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THE THYROID INFLUENCE ON THE BEHAVIOR OF THE WHITE RAT

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DISSERTATION

PRESENTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE GRADUATE SCHOOL OF THE OHIO STATE UNIVERSITY

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Reprinted from COMPARATIVE PSYCHOLOGY MONOGRAPHS
Vol. II, No. 12, May, 1925

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From the Psychological Laboratory of the Ohio State University

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ACKNOWLEDGMENTS

This occasion is taken to acknowledge the assistance of Dr. A. P. Weiss who has supervised the planning and experimental stages of this monograph. To Prof. R. G. Hoskins of the Department of Physiology, I am indebted for advice on the endocrine aspects of the experiment; to Prof. R. C. Osburn and W. M. Barrows of the Department of Zoölogy for room, and to Prof. G. F. Arps for the administrative courtesies so essential in securing apparatus and the maintenance of favorable conditions for animal experimentation.

I wish to acknowledge my obligation to Dr. F. S. Hammett of Wistar Institute, Philadelphia, for assistance given during preliminary work on the problem and to Miss Louise Duhring of the same institution who gave valuable advice in the preparation of the conditions for successfully rearing a large colony of animals.

I. INTRODUCTION

The present investigation was directed toward establishing the effect of modification in thyroid gland functions upon the learning ability of the albino rat. The importance of the internal secretions upon the physiological processes is at present recognized by the branch of physiology known as endocrinology and this experiment was undertaken as an extension of this type of investigation into the field of animal behavior. That the results would have some value in the explanation of some forms of abnormal human behavior was my hope, and accounts partly for the fact that it was developed in a psychological atmosphere—although that of behavioristic psychology.

The rat was selected as a subject because its anatomy, physiology, and behavior are better known than that of any other animal. Donaldson (23) has reported complete findings on the growth and anatomical conditions; the normal development of the rat, as a subject for experimentation, has been extensively treated by Huber (64) who has also reported the embryological development from conception to birth. There are, therefore, excellent norms available for checking and verifying the different

phases of the life cycle, making possible accurate differentiations between the normal and abnormal conditions in growth and development that may result under experimental conditions.

I have selected the thyroid gland as the endocrine organ whose effects on behavior are to be studied, because its physiological function and anatomical structure are better known (with the possible exception of the adrenal) than any other of the so-called ductless glands. While much has been written on the pathological conditions that result from thyroid excess or insufficiency, the effects of these conditions on behavior, such as that which is represented by learning capacity, have received practically no attention.

II. PROBLEM

The word "behavior" in the title which I have chosen for this paper, promises more than it seems to me is warranted from the results which I hope to present, yet I justify its use by the ambiguity which is associated with the term behavior. I have actually tried to measure the influence of various thyroid conditioned on maze learning, but so many other factors were modified which could not be designated as learning that I felt obliged to extend the scope of the title, by substituting the word behavior for learning.

What I have tried to do can better be understood from an examination of the following outline which gives the interrelations between the three thyroid conditions that I have investigated and the maze learning of the rats. The study has been divided into three experiments as follows:

Experiment I. Effect of thyroidectomy on maze learning:
1. As dependent on age of the operated animals
2. The offspring of operated animals

Experiment II. Effect of injecting thyroid gland substance on maze learning in normal animals:
1. As dependent on age
2. The offspring of injected animals

Experiment III. Effect on maze learning of feeding thyroid gland substance to normal animals:

1. As dependent on age
2. The offspring of "fed" animals

With this abridged outline of the nature of the investigation, I will pass to a brief résumé of the literature on the subject before beginning the detailed report of the experiments.

III. LITERATURE

The thyroid gland has been recognized as a distinct part of the body for the past three centuries. At first an object solely of theoretical interest whose functions were to be derived from the logical considerations of man's needs, the thyroid gland gradually became the object of that rigorous scrutiny which characterizes what we now designate as the scientific method.

As early as 1650 in Handfield-Jones' (54) translation of Galen's work, it is supposed that the glands of the larynx have been created for the purpose of moistening and bathing all parts of the larynx and passage of the throat. The ductless character of the thyroid gland is indicated in this same work by the statement, "the neck has two glands in which a moisture is generated: but from the two glands which are in the neck there come forth no vessels by which the moisture may flow out, as those do from the glands of the tongue" (p. 346). Wharton (122) in 1656, according to Vincent (110) gives an account of the anatomy of the thyroid and calls attention to the fact that it is much more distended with blood, more viscid, and more solid than any other gland. Its structure is described as glutinous rather than fibrous. Four functions are assigned to the gland:

. . . . the first and principal use of these glands appears to be to take up certain superfluous moistures from the recurrent nerve, and to bring them back again into the vascular system by their lymph channels. Second, to cherish the cartilages to which they are fixed, which are rather of a chilly nature, by their own heat; for they are copiously supplied with arteries, and abound with blood, from whence they may conveniently impart heat to the neighboring parts. Third, to conduce by their exhalations to the lubrication of the larynx and so to render the voice smoother, more melodious, and sweeter. Fourth, to contribute

much to the rounded contour and beauty of the neck; for they fill up the empty spaces about the larynx, and make its protuberant parts almost to subside and become smooth, especially in the female sex, to whom on this account a larger gland has been assigned, which renders their necks more even and beautiful.

Morgagni (85), in 1718, described the vesicular cavities in enlarged thyroids, and these he supposed to be normal vesicles distended by the accumulation of their secretion. Santorini (93) in 1724, fails to find a duct but thinks that the thyroid gland may be forced to expell its secretion by a contraction of an overlying muscle. Thus as early as 1724 the thyroid is classified as a gland without a duct, which secretes a special fluid that is received into the veins and so introduced into the general circulation of the blood and the lymph. The earlier or pre-scientific speculations on the functions of the thyroid gland may be regarded as coming to a close with Santorini's work.

A new period in which speculation was superceded by experimental extirpation and the feeding of the gland marked the beginning of new methods. However, most of the experiments performed during the later half of the eighteenth and earlier part of the nineteenth centuries seemed to be of little significance.

Bardeleben (5), in 1844, found that extirpation of the thyroid gland had little effect on dogs and rabbits. Schiff (96) in 1859, found that the extirpation method gave variable results for rabbits, rats, and cats. Some animals were able to survive and others died as a result of the operation. In 1884, he repeated these experiments (97, 98, 99) and found that thyroidectomy in rats and rabbits was not followed by any serious result. In the dog and cat complete removal was fatal. The symptoms noted in these cases were general malaise, troubles of locomotion, alteration in sensibility and vaso-motor disturbances. These results were confirmed by Colzi (13) and Wagner (116) in 1884, Welch (120) in 1888, Fuhr (32, 33) in 1886 and 1889, Ewald (29, 30) in 1887 and 1889 and von Eiselsberg (115, 116) in 1893 and 1894.

Philipeaux (89) and Drobnick (24) in 1884 and Munk (87) in 1887 found that the animal could survive the removal of the gland and attributed the death of the animals of the other in-

vestigators to the injury of the nerves and reflex centers instead of to the removal of the gland. Gley (34, 43) carried on experiments between 1892 and 1911 in which he found that the entire removal of the thyroid-parathyroid apparatus was followed by death in almost every case but that the removal of the thyroids alone was not fatal.

Vassali and Generali (107) in 1894 and 1900 confirmed Gley's results. Jolly and Vincent (11–112) in 1904 and 1906 found that removal of the parathyroids was fatal even when the thyroid was left intact, but that the animal could survive the removal of the thyroid. Vassali and Generali (108) in 1900 were the first to show that the aqueous extract of the desiccated or raw thyroid gland when injected intravenously was able to neutralize the marked effects of thyroidectomy.

The function of the thyroid gland has been studied indirectly in connection with work on other parts of the body. Loeb (79) reports a loss of weight following the extirpation of the gland. In feeding thyroid substance but without extirpating the gland: Farrant (31) and Moussu (86) report large doses toxic; small doses are reported as stimulating growth by Moussu (86); with dosage unspecified, Cunningham (15) found no effect, Lenhart (74) found retarded growth, and Magnus-Levy (82) reports decreased metabolism.

All of the observations thus far indicate that the thyroid system very probably exerts a strong influence on the general behavior of the organism, and this is indirectly studied by von Eiselsberg (116) who finds that nervous symptoms such as lethargy and mental dullness follow extirpation.

Direct experimental results bearing on the relation between the thyroid mechanism and behavior are not numerous. Dr. F. S. Hammett has reported many studies which are directed toward ascertaining the physiological effects and among these studies frequent behavior references are found. He found (47) that when the rat has been handled continually it loses its fear of human beings, and its behavior is changed from a condition of excitability and irritability which is expressed by flight and pugnacity to a state where these reactions are reduced to in-

significance and the animal will be completely relaxed when taken up. This process Hammett designates as "gentling." He found (48) that in the animals that had not been gentled 79 per cent die of acute parathyreopriva within forty-eight hours after parathyroidectomy, while in animals that have been gentled only 13 per cent fail to live. From a study of the effects of thyroid and parathyroidectomy on growth in body length, weight and tail length of male and female albino rats (49) he reports

> an examination of the effects on growth in body length, body weight and tail length of male and female albino rats deprived of the thyroid and parathyroid, or parathyroid glands alone at 100 days of age and allowed to grow until 150 days of age has been made. Both males and females responded qualitatively alike to the loss of the functions of these glands of internal secretion. The response was a retardation in growth of the parts measured. From the quantitative standpoint the growth of the females was retarded or obstructed to a greater degree by the experimental procedures than was that of the males. It would appear from this that the female rat is more dependent upon the stabilizing influence of the thyroid and parathyroid glands than are the males. Growth in body weight was inhibited to a greater extent than was growth in body length and tail length after the loss of either the parathyroid or thyroid or of both. This is taken to indicate that cell growht by accretion is more susceptible to disturbing factors than is growth by cell division. . . . . On the other hand the retardation of growth following thyroid removal is not a poisoning of the organism, ... but is an actual diminution in the ability to grow due to the loss of a major stimulus to growth and metabolism.

Liddell (76) gives a preliminary report of an investigation of thyroidectomy on sheep. He operated three pairs of twin lambs and found that the operated animals had much more difficulty learning a simple labyrinth than those which had not been operated. He later reports (77) further investigations on the effects of thyroid extirpation on the neuro-muscular mechanism of lambs. In this study two aspects of the neuromuscular conditions of the thyroidectomized animals were particularly observed: (*a*) spontaneous activity, and (*b*) muscular power.

a. The spontaneous activity of the animals was estimated by the use of a pedometer which was fastened to the leg of the sheep and left in place while the animal was in pasture and roaming about over the field with no especial stimulus to activity. This method of measuring was found to be of doubtful reliability in its effectiveness to really measure differences in the activity of the normal and operated sheep. The operated sheep would follow the flock about over the field and the shorter leg length of the thyroidectomized sheep also introduced a pedometer error very difficult to correct.

b. In measuring the differences in muscular power between the operated and normal animals, an inclined plane was used. This plane led into the food box and all animals had to pass over it to obtain their food. The inclined plane was raised until the operated animals were unable to climb up after the other animals. The instinct of a sheep to follow a leader served as a stimulus to activity when food failed as a stimulus. Quantitative results were withheld for further observation and experimentation.

There are at present few studies available on the reliability of data secured from the various types of mazes. Of these two may be mentioned, Heron (54a) working with an electrical maze on human subjects finds

> that the larger the groups considered, the greater the probability that the averages of such groups will represent differences in maze learning ability, for the larger the group the greater is the range over which chance may operate and still not displace the individual from the group in which his particular degree of activity would place him.

Hunter and Randolph (65a) report similar findings with reference to the reliability of individual performance in maze learning problems.

With this brief presentation of the literature bearing on our problem we pass to the report of the present experiment.

IV. PRELIMINARY EXPERIMENTATION

Before undertaking the major experiments to determine the effect of thyroidectomy upon learning capacity, it was necessary

to perform preliminary experiments on the effect of the thyroid gland substance[1] on normal animals, under conditions such as the following: (*a*) the effect of feeding the substance, (*b*) how much of the substance could be fed or injected (tolerated) without marked changes in behavior or physiological conditions.

1. Preliminary feeding of thyroid gland substance. Ascending series

Influence of gradual increment in the feeding of T. G. S. to animals of different ages.

Five groups of 10 animals each were selected, aged respectively 26, 40, 50, 60 and 100 days. They were placed in individual cages and given the T. G. S. (in powdered form) mixed with milk. The rats ate this food readily, even though it was followed by sickness and death. In each case the initial amount given was 0.01 gram. This amount was gradually increased until the animal died.

Ascending from 26 days

Ten normal animals 26 days of age were fed T. G. S. at an ascending rate of 0.05 gram per day, beginning with 0.01 gram for the first day and continuing to 0.65 gram.

The results are as follows:

TIME	DOSE	RESULT
days	*gram*	
26–32	0.01–0.30	Health normal
32–34	0.35–0.40	Refused regular ration of food, no other symptoms noted
34–36	0.40–0.50	Refused food, became weaker, pulse faster
36–38	0.50–0.60	Progressively weaker, pulse faster, muscular spasms
39	0.65	Fatal to all animals

[1] The desiccated thyroid gland was obtained from Parke, Davis and Co. It was guaranteed to contain 0.2 per cent iodine and 1 grain of the powdered substance represented 5 grains of fresh thyroid gland. In this report the abbreviation T. G. S. refers to this substance.

Conclusions. With normal animals 26 days old no harmful effects of T. G. S. feeding were detected until the daily amount was 0.30 gram. The fatal dose was 0.65 gram. After this, abnormal symptoms became noticeable and the animals deteriorated very rapidly.

Ascending from 40 days

Ten normal rats 40 days of age were fed T. G. S. at an ascending rate of 0.05 gram per day, beginning with 0.01 gram for the first day. When the dose given was 1.00 gram the rate was increased to 0.50 gram per day.

The results are as follows:

TIME	DOSE	RESULT
days	*grams*	
40–50	0.01–0.60	Health normal
52–56	0.60–0.80	Refused regular ration of food, no other symptoms noted
56–59	0.80–0.95	Refused food, became weak, pulse increased
59–63	0.95–2.00	Progressively weaker, extremely rapid pulse
63–65	2.00–3.50	Very weak, extremely rapid pulse, muscular spasms, vomiting
66	4.00	Fatal to all animals

Conclusions. With normal rats 40 days old no harmful effects of T. G. S. feeding were detected until the daily amount given was 0.60 gram. The fatal dose was 4.00 grams. After the 59th day the abnormal symptoms increased very fast and the deterioration was very rapid.

Ascending from 50 days

Ten normal animals 50 days of age were fed T. G. S. at an ascending rate of 0.05 gram to the 70th day when an increase by 0.50 gram daily was made. Feeding began with 0.01 gram.

The results are as follows:

TIME	DOSE	RESULT
days	*grams*	
50–62	0.01–0.60	Health normal
62–68	0.60–0.90	Weak and refused food
68–72	0.95–2.00	Refused food became weak, pulse increased, muscular twitching, increased respiration
72–74	2.00–3.00	Very weak, rapid pulse, vomiting, spasms, diarrhea
74–77	3.00–4.50	Symptoms same as above, increased weakness
78	5.00	Fatal to all animals

Conclusions. With normal animals 50 days old no harmful effects of thyroid feeding were noted until the daily amount given was 0.60 to 0.90 gram. The fatal dose was 5.00 grams. Following the 72nd day the deterioration symptoms increased with great rapidity, to death on the 78th day.

Ascending from 60 days

Ten normal animals were fed T. G. S. at an ascending rate of 0.05 gram, to the 20th day when the daily amount was increased to 0.50 gram. The amount given on the first day was 0.01 gram.

The results are as follows:

TIME	DOSE	RESULT
days	*grams*	
60–75	0.01–0.75	Normal health
76–79	0.80–0.95	Refused food, no other symptoms noted
80	1.00	Refused food, rapid pulse, muscular twitching
81–87	1.50–4.50	Refused food, rapid pulse, muscular spasms, increased respiration
88–93	4.50–7.50	Symptoms same as above, with vomiting and diarrhea
94	8.00	Fatal to all animals

Conclusions. With normal animals 60 days old no harmful effects of thyroid feeding were noted until the daily amount given was 0.80 gram. The dose fatal to all was 8.00 grams. Deterioration was great after the 81st day. However the animals continued to live until the 94th day.

Ascending from 100 days

Ten normal animals 100 days old were fed T. G. S. at an ascending rate of 0.05 gram per day to the 19th day when the dose was increased 0.50 gram daily. The initial dose was 0.01 gram.

The results are as follows:

TIME	DOSE	RESULT
days	*grams*	
100–114	0.01–0.75	Health normal
115–118	0.80–0.95	Refused food, no other symptoms noted
119	1.00	Refused food, became weak
120–127	1.50–5.00	Refused food, became weaker, increased respiration, rapid pulse
127–131	5.00–7.00	Extreme weakness, increased pulse, vomiting diarrhea, increased respiration
132	7.50	Fatal to all animals

Conclusions. With normal animals 100 days old no harmful effects of thyroid feeding were noticed until the dose was 0.75 gram daily. The fatal dose was 7.50 grams for all animals. Symptoms increased very rapidly after 120th day, after 127th day the deterioration of the animals was extremely rapid to death on the 132nd day.

Table 1 gives a summary of the experiment to determine the influence of a daily increment of the amount of T. G. S. for rats at ages given. With the legend the table largely explains itself, but the following items should be noted:

1. The amount of T. G. S. causing death varies from 0.65 gram for the 26-day-old rats to 8.00 grams for the 60-day-old rats.

2. The amount given when symptoms of weakness first appear is the same for 60- and 100-day-old rats.

3. In 60- and 100-day-old rats, 10 animals of each group gave same symptoms on the same day (probably a more homogeneous group).

4. The 26-day-old animals died 13 days earlier as a result of T. G. S. feeding than did the 40-day-old animals.

5. Inactivity and weakness appear 6 to 8 days earlier in the 26-day-old rats than in the older groups following.

Having determined the conditions under which the feeding of T. G. S. proved fatal or produced the physiological effects indicated, the next preliminary step was to determine the dose of the T. G. S. which could be given and maintain apparently normal function. This condition we have designated as the amount of T. G. S. that is "tolerated."

TABLE 1

Summary of results of preliminary feeding of T. G. S.

A	B	C	D	E	F	G
26	33–34	6–8	0.35–0.40	39	13	0.65
40	52–53	12–13	0.60–0.65	66	26	4.00
50	63–64	13–14	0.65–0.70	78	28	5.00
60	75	15	0.75	94	34	8.00
100	114	14	0.75	132	32	7.50

A, age at which T. G. S. feeding was started.

B, age at which inactivity and weakness first appeared.

C, days after feeding at which inactivity and weakness appeared

D, amount of T. G. S. being taken at first appearance of inactivity and weakness.

E, age of animals at which death occurred.

F, days after feeding at which death occurred.

G, amount of T. G. S. given at time of death.

2. Toleration of T. G. S.

Toleration by feeding T. G. S.

Five groups of 5 normal animals each, ages 26, 40, 50, 60, and 100 days were fed the amounts of T. G. S. which caused the refusal of food in the groups reported in table 2. The first feeding was sufficient to cause the animals to refuse their food on that day and the amount of the dose was then decreased by 0.10 gram and the feeding continued at this rate for four days. Table 2 which follows herewith gives a summary of these experiments.

With the legend the results of the tables are largely self-explanatory but the following items deserve special mention:

1. The 26 to 40-day-old animals showed an enlarged thyroid which was almost three times its normal size.

2. The amount of T. G. S. tolerated varied from 0.30 gram for the young animals to over twice this amount for the 60- and 100-day-old rats. Roughly this shows an increase of toleration with age up to about 60 days.

Toleration by injecting T. G. S.

Ages 26, 40, 50, 60, 100 days

In order to extend the range of the conditions under which the T. G. S. may become effective, the feeding of the extract

TABLE 2

Summary of toleration by feeding T. G. S.

H	I	J	K	L	M
36	36	0.40	0.30	31	Enlarged
40	40	0.60	0.50	44	Enlarged
50	50–51	0.70–0.60	0.60	55	Normal
60	60–61	0.80–0.70	0.70	65	Normal
100	100	0.80	0.70	105	Normal

H, age at beginning of feeding T. G. S.
I, age at which rats refused to eat and were weak.
J, amount of T. G. S. given first day.
K, amount of T. G. S. tolerated.
L, age at autopsy.
M, condition of gland at autopsy after five days feeding.

was supplemented by a preliminary experiment in which the T. G. S. was injected into the blood stream. A 20 cc. Luer hyperdermic syringe with a 00 size needle was used for the injections. The T. G. S. was mixed with water so that it would flow through the needle readily. This mixture was injected into the femoral artery. Previous to the injection the spot on the inside of the leg where the artery runs close to the skin was washed with iodine, the needle was thrust through the skin and the solution forced into the blood stream. The amount used at first was half the amount given by mouth feeding and the dose was increased until the animals showed muscular spasms

and an increased pulse. Then the dose was decreased until the animal's condition improved. After the condition was normal to observation, the dose was repeated for five days.

Five groups of ten normal animals each, ages 26, 41, 51, 61, and 101 were injected with the amounts of T. G. S. indicated in Table 3 which follows herewith and gives a summary of the results. With the legend the table is self-explanatory.

The older animals could tolerate larger amounts of T. G. S. than the younger animals; the 101-day-old group being able to tolerate more than twice the amount of the 26-day-old group,

TABLE 3

Summary of toleration by injecting T. G. S.

N	O	P	Q	R	S
26	28–29	2–3	0.2–0.3	0.15	0.15
41	43–48	3–7	0.35–0.5	0.25	0.25
51	53–56	2–5	0.35–0.5	0.30	0.30
61	63–66	2–5	0.4–0.6	0.35	0.35
101	103–104	2–3	0.45–0.5	0.35	0.35

N, age at beginning injection.

C, age at which rats refused to eat, had muscular spasms and increased heart beat.

P, days after injection rats refused to eat, had muscular spasms and increased heart beat.

Q, amount injected when rats refused to eat, had spasms and increased heart beat.

R, amount of T. G. S. tolerated.

S, amount of T. G. S. injected on first day.

without showing any of the symptoms of languor, loss or increase of appetite and hyperactivity.

3. Summary of preliminary experiments

Table 4a gives in condensed form the results of the feeding of T. G. S. until death occurred. It is worthy of mention here that the animals were able to tolerate more and more of the T. G. S. as they became older. The 60-day-old group were able to take the maximum amount of T. G. S. and death occurred almost three times later than that of the 26-day-old group.

Table 4b shows the summary of the toleration experiment. The animals were able to tolerate twice the amount of T. G. S. when it was fed by mouth than when it was given by injection.

V. APPARATUS USED FOR TESTING LEARNING

A simplified form of the Watson Circular maze (119) was used for testing the learning ability of the rat. A diagram (figs. 1–2) of the maze used is given with a description. The original Watson maze was simplified by making fewer blind alleys for the animal to avoid. The work of Dashiell (19, 21) seemed to show that a decrease in the number of choices which the animal had to make decreased the complexity of the animal's reaction. Working

TABLE 4a

Feeding T. G. S.—ascending series

	AGE FEEDING STARTED				
	26	40	50	60	100
Age first languor and inactivity appear.	33–34	52–53	63–64	75	114
Days after feeding above appear.....	6–8	12–13	13–14	15	14
Amount of T. G. S. given when above appear.....	0.35–0.5	0.75–0.9	0.75–0.9	0.95	0.95
Age at death.....	39	66	78	94	132
Days after feeding, death occurred.....	13	26	28	34	32
Amount of T. G. S. given at death.....	0.65	4.00	5.00	8.00	7.50

from this conclusion, I decreased the difficulty of the maze by decreasing the number of choices. With this maze I hoped to secure a controlled environment and to determined from the variability of the reactions what the effects of the thyroid gland variable would be.

The Yerkes-Kellogg (25) double reflection method (fig. 2) of recording maze reactions was used. This consisted of a large mirror placed over the maze at a forty-five degree angle; the reflection of the maze in the mirror was thrown through a lens upon a small mirror which reflected the maze onto a glass in the table top. This table was covered with a black sateen hood to keep out all light and to provide an opportunity for observing the animals as they moved about in the maze.

TABLE 4b

Toleration experiments, feeding and injecting

	FEED	INJEC-TION	FEED	INJEC-TION	FEED	INJEC-TION	FEED	INJECTION	FEED	INJECTION
Age at starting of experiment	26	26	40	41	50	51	60	61	100	101
Age rats refused to eat	26	28	40	43	50	53	60	63	100	103
Amount of T. G. S. first day	0.40	0.15	0.60	0.25	0.70	0.30	0.80	0.35	0.80	0.35
Age-increased respiration		28		44–47		53–55		63–65		103–104
Age-increased pulse spasms		28		44–47		53–55		53–55		103–104
Amount of extract tolerated	0.30	0.15	0.50	0.25	0.60	0.30	0.70	0.35	0.70	0.35
Amount of extract when rats refused food	0.40	0.30	0.60	0.40	0.70	0.4–0.5	0.80	0.45 0.60	0.80	0.45-0.50
Condition of gland at autopsy	Enl.*		Enl.		Nor.†		Nor.		Nor.	
Age at autopsy	31		45		55		65		105	

* Enlarged.

† Normal.

The whole room was darkened when the rats were placed in the maze; this was done for two reasons, first because the glare of sunlight on the maze destroyed an accurate view of the animals' maze through the lens system and second because the animals were more active in the maze when artificial light was used. This double-reflection method had an added advantage which has not been mentioned before, in that the observer was several feet away from the animal while it was working in the maze. The animals had a tendency to stop in front of the observer or any other person near the maze, rather than to attempt to

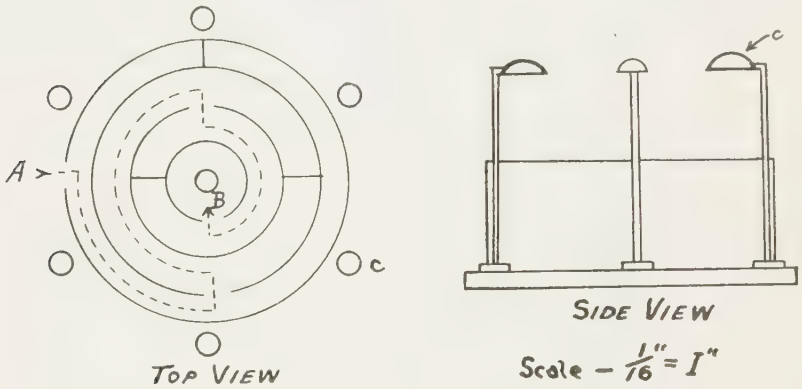

FIG. 1. *Top view of maze,* 80 cm. in diameter, alleys 10 cm. wide. *A* to *B*, 480 cm., true path into maze. *c*, electric lights (40) watt arranged around edge of maze with one in center.

Side view of maze: Sides of maze, 10 inches high, light standards of three-fourths inch pipe with green reflectors over the light bulbs.

continue their way through the maze. This tendency of the animals might be accounted for by the fact that I had handled the animals as much as possible in order to destroy any possible effects of excitation on the operated animals which might change their behavior in the maze.

The rats were given their ration of food in the center of the maze for three days preceding that on which they were first put at the entrance of the maze for their first trial. After these three days the animal was placed in the entrance box and allowed to find its way to the center. When it reached the center it was

allowed to eat before being removed; the food given at this time was the regular ration, to which was added some delicacy which was given at no other time.

Later in the experiment when food seemed to fail as a stimulus for the thyroidectomized animals or their offspring, an attempt

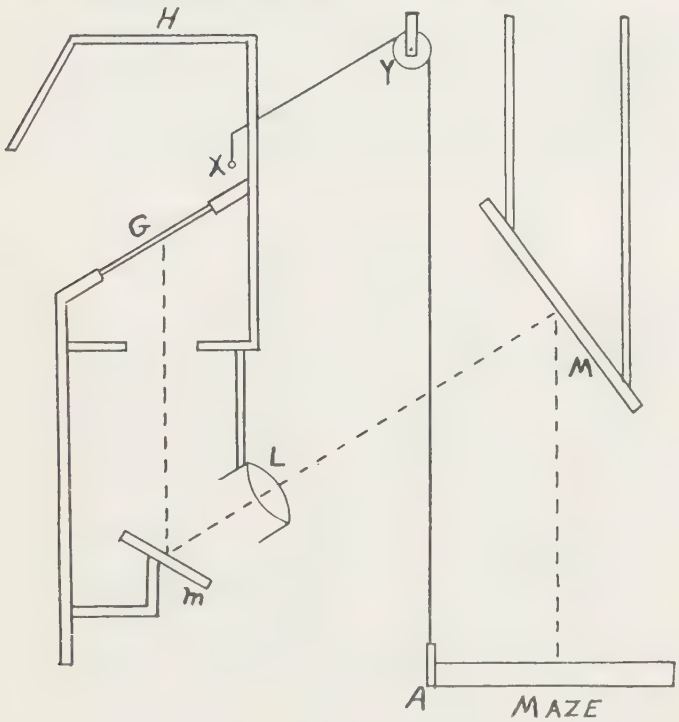

FIG. 2. M_1, Plate glass mirror, 36 inches square, hung at 45 degree angle over the maze. Distance M to m, through lens L equals 20 feet. X m, Mirror 8 inches by 6 inches which reflected maze on to ground glass, G, in table top. H, Hood of black light proof sateen. Cord attached from table over pulley, Y, to raise partition A separating entrance box from maze.

was made to use the sex instinct as a stimulus. The animal was placed in the center of the maze with a normal animal of the opposite sex and left there for a short time, five to twenty minutes; then the subject animal was placed in the entrance to the maze as usual. This procedure did not seem to have the desired stimulating effect.

A record of the time in seconds which the animal required to go from the entrance to the center was kept and a few typical tracings of the ramblings of the operated and "thyroid fed" animals in the maze were made.

VI. CRITERIA OF LEARNING ABILITY

When the animal had learned to run the maze in sixty seconds without errors on the way, the maze was considered completely learned. Time only was considered. The object was not so much to establish individual differences but to compare the attainments of groups with one another.

VII. THYROIDECTOMY TECHNIQUE

Anesthesia and binding

The method of extirpating the thyroid mechanism was practically the same as that followed by Cristiani (16) and by Hammett (47, 48, 49, 50) in his recent studies on the thyroid apparatus.

This procedure is as follows: Animals which, from observation exhibited a normal state of health and activity were selected. During the twenty-four hours previous to the operation no food was given. At the time of the operation the rat was placed in a large jar with a glass cover. A small dish containing a mixture of one part chloroform to three parts of ether was placed in the jar with the animal. It required about thirty seconds for the animal to become completely anesthetized. During this time the rat would move slowly about and just before succumbing entirely would make frantic efforts to escape from the jar.

Other methods of anesthetizing the animals were tried but without the success that accompanied the method finally adopted.

An operating board was especially prepared for use in this work. The board, 1 inch thick by twelve inches long and eight inches wide, was fitted out with eight brass hooks about $\frac{1}{2}$ inch in height. These were placed in two rows of four hooks each extending along the sides of the board for 6 inches. Two holes were bored between the first two hooks, a tape was knotted and passed up through the holes on either side to be hooked under

the incisor teeth of the animal. This served to hold the head back and stretch the neck muscles taut. This tape was brought down across the rat from hook to hook in such a manner as to hold back the forelegs and completely bind the animal to the board.

This procedure of anesthetizing the animal and binding it to the board took on the average three minutes. With the exception of a slight twitching of various muscles after the animal had become completely anesthetized, it made no movements until it revived about thirty or forty seconds after the completion of the operation.

Thyroidectomy

In beginning the operation, a longitudinal incision of about $\frac{1}{2}$ inch in length was made posteriorly from just beneath the jaw bone. The skin was drawn back and held by means of a small clamp attached to each side, this made a diamond shaped opening.

Starting at the top of the incision and working carefully downward, the neck muscles were separated longitudinally in such a manner as to prevent unnecessary injury to them. These muscles were held apart by fastening two hemostats just above the clamps which held back the skin and thus a large space was provided for working. As the animals were all in good condition there was an abundance of fat tissue about the neck. This was removed exposing the trachea which extended along the floor of the incision. The thyroid gland was found about the middle of the floor of this opening. It consisted of two lobes lying laterally to the trachea. The thyroid tissue is ligher in color than the surrounding material. When the thyroid is separated from the trachea, the parathyroid appears, it is yellowish white with a slight pink tint. The superthyroid artery was tied off with a gut ligature and this was left in place when the incision was closed. The thyroid gland was clipped off carefully and stripped from the parathyroid. (It was impossible, of course, to avoid disturbing the parathyroid slightly, but in those cases in which it was injured sufficiently to produce symptoms of parathyroid tetany as given by Dr. Hammett (48) or death within

forty-eight hours, the results were not used in the preparation of records.)

Following the operation, the incision was closed and washed over with cresote and in all but three cases healed by first intention. Three animals died two days following the operation with symptoms of weakness and the incision had become suppurative.

The whole process, giving the anesthetic, binding and operation took about six minutes.

VIII. EXPERIMENT I

1. The effect of thyroidectomy on maze learning

In this experiment the effect of extirpation of the thyroid gland will be considered with respect to age and the effect on the progeny. The preliminary toleration experiment indicated that age was an important factor and must be controlled. The effect of thyroidectomy on the progeny of the first and second generation is also considered with respect to treatment with T. G. S.

Normal animals were thyroidectomized at different ages, both before and after learning to run the maze within the minimum limit of 60 seconds. The animals were allowed ten days to recover from the effects of the operation with the exception of one group which was allowed but five days for convalescence. In all cases the incision was entirely healed before the animals were placed in the maze.

Normal control series (no thyroidectomy)

Ten normal animals were used.

	days
Maze learning	31 to 40
Rest interval	41 to 50
Maze learning	51 to 60
Rest interval	61 to 65
Maze learning	66 to 75

Ten normal animals 31 days of age were placed in the maze, and passed from the entrance to the food box in the center. The average time for running the maze decreased from 120

seconds on the first day to 60 seconds on the ninth and tenth day as shown in table 5a. Sixty seconds, it will be remembered, was taken as the time which indicated that the true path had been completely learned.

These animals were then given a ten-day rest interval between the 41st and 50th day so that their training would correspond with that of the thyroidectomized animals later on. The results after the ten-day rest interval are shown in table 5b.

TABLE 5a

	AGE									
	31	32	33	34	35	36	37	38	39	40
Trial	1	2	3	4	5	6	7	8	9	10
Average time	120	103	99	93	89	83	80	70	60	60

Average of 10 trials, 80 seconds.

TABLE 5b

	AGE									
	51	52	53	54	55	56	57	58	59	60
Trial	11	12	13	14	15	16	17	18	19	20
Average time	89	84	82	78	70	60	60	60	60	60

Average of 10 trials, 70 seconds.

TABLE 5c

	AGE									
	66	67	68	69	70	71	72	73	74	75
Trial	21	22	23	24	25	26	27	28	29	30
Average time	75	76	70	70	60	60	60	60	60	60

Average of third 10 trials, 65 seconds.

This average time decreased from 89 seconds on the first day after the interval (11th trial) to 60 seconds on the 16th trial and remained at this minimum for the rest of the period. The average time for the second ten trials (11 to 20) is 70 seconds or ten second less than for trials 1 to 10.

The animals were then kept out of the maze for a second interval between the ages of 61 and 65 days and when returned ran the maze as indicated in table 5c.

It is to be noted that the average time decreased from 75 seconds on the first day (trial 21) and reached the 60-second minimum by the fourth day (trial 24). The average time for the third ten trials (21 to 30) is 65 seconds.

In order to give a running picture of the results, the tables 5a, b, c, have been reduced to figure 3, which follows and which practically explains itself. The graph of this control series

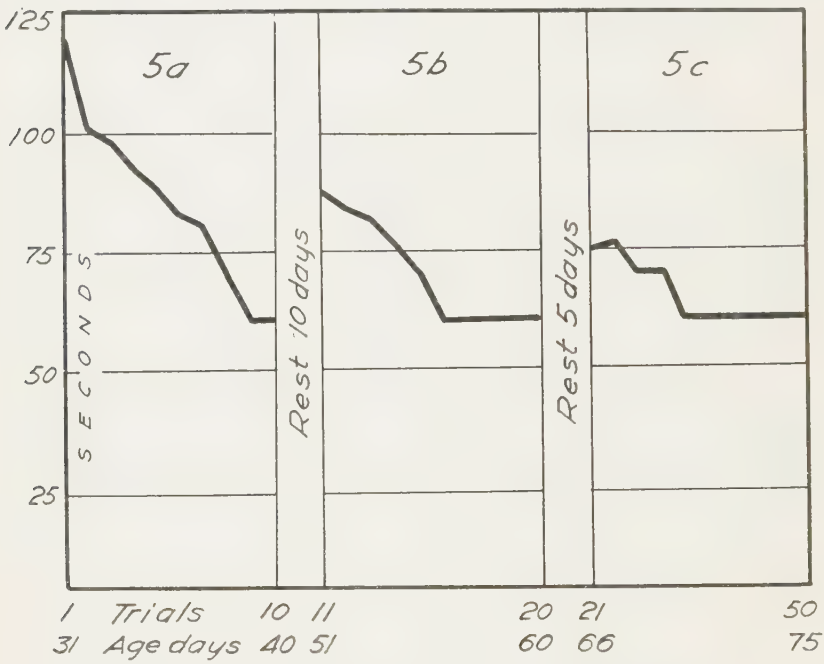

Fig. 3. Graphic Representation of Tables 5a, b, c

shows a consistent improvement which is evident in the work of the normal animals in the maze. Trials 1 to 10 show a typical learning curve. After ten days rest (41 to 50) the average of the first trial (11) after the rest starts at 89 seconds, about the same as trial 5 of the first period. After the second rest period of five days (61 to 65) the rats start at an average of 75 seconds which decreased to complete learning on the 5th trial of the period or the 25th trial of the series. The curve

shows a fairly consistent downward slope from the first day of training to the 30th day. The two sharp elevations at the beginning of each learning period are also indicative of what would be expected if practice is interrupted.

The results indicated in the tables 5a, b, c and figure 3, will be the standards with which the other experimental conditions will be compared. The behavior of the animals during this period will be considered as normal, they ran the maze steadily, and fast. The movements were stable and well directed, the sensitivity was normal in all respects, both vitality and capacity to learn were normal and in all cases the ability to accurately run the maze increased from day to day as shown by the decrease in the time taken. In some of the graphs which follow, a normal control level is indicated. This is taken from this 5a, b, c series unless otherwise indicated. It is not always possible to get a complete coincidence as regards age, number of trials, number of rest periods, between the experimental series and the control series. Because of this fact the control conditions are sometimes schematized to meet the experimental conditions.

Effect of extirpation

Thirteen normal animals were used.

	days
Maze learning	30 to 39
Thyroidectomy	39th
Convalescent period	40 to 49
Maze learning	50 to 69

The results of the maze learning before the thyroidectomy are given in table 6a.

A comparison of these results with those from the control group (table 5a) shows these animals to be normal in their ability to learn the maze, the average time for the first ten trials being 79 seconds as compared with 80 seconds for the control group.

On the 39th day the thyroid gland was removed and the animals allowed to recover or convalesce for ten days. One animal died during the operation; two more, two days after the operation.

Resuming the maze learning on the 50th day of age and continuing for 20 days, the results are shown divided into two periods: Table 6b from the 50th to the 59th day; table 6c from the 60th to the 69th day.

On the 15th trial one rat failed to leave the entrance box and again on the 19th day this animal made no attempt to run the maze. Another rat failed on the 20th trial. The results in-

TABLE 6a

	AGE									
	30	31	32	33	34	35	36	37	38	39
Trial	1	2	3	4	5	6	7	8	9	10
Average time	112	97	92	87	82	70	70	60	60	60

Average of 10 trials, 79 seconds.

TABLE 6b

	AGE									
	50	51	52	53	54	55	56	57	58	59
Trial	11	12	13	14	15	16	17	18	19	20
Average time	90	104	122	145	376	253	305	365	565	665

Average of 10 trials, 303 seconds.

TABLE 6c

	AGE									
	60	61	62	63	64	65	66	67	68	69
Trial	21	22	23	24	25	26	27	28	29	30
Average time	830	890	1,090	1,440	1,570	1,350	1,580	1,830	1,488	1,890

Average of 10 trials, 1396 seconds.

dicate very clearly that the effect of the thyroid extirpation is to eliminate the effects of maze learning.

The further deterioration of the learning ability and also the loss of what has been already learned in these animals is shown in the second half of the post-operative results as indicated in table 6c.

At trial 21 the rat that failed on the 20th trial again failed. It will also be noted that the average time for trials 21 to 30,

(1396 second) is over four times as long as the average time (303 seconds) of the preceding ten trials 11 to 20.

In order to give a continuous picture of the results, the condensed tables 6a, b, c, has been represented by figure 4, which

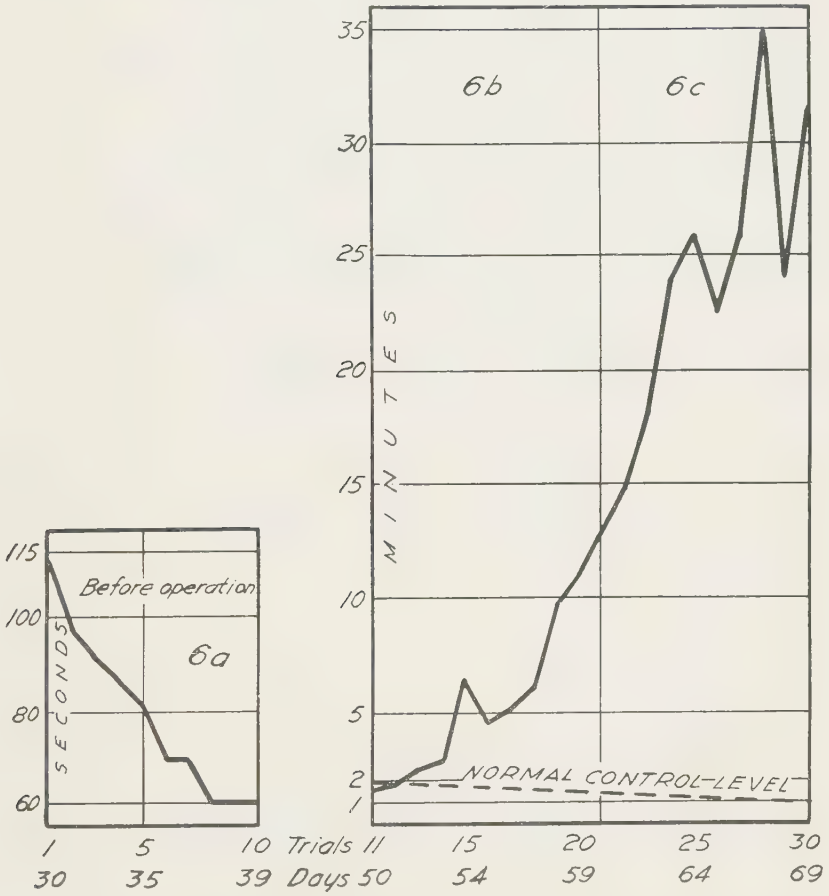

Fig. 4. Graphic Representation of Tables 6a, b, c

follows and which practically explains itself. It should be noted that the time for 6b and 6c is given in *minutes* and the effects when compared with the normal period (Curve 6a) which is given in *seconds* should be multiplied 60-fold. That is to say, 6a

placed on 6b and 6c is practically the dotted straight line indicated between the 1- and 2-minute time levels.

The curves show that during the normal period the animals show the characteristic decrease in the time spent in traveling through the maze while the movements of these same animals, with the thyroid removed, gradually become slower and more meaningless until they have practically lost their ability to go through the maze. The action of all animals on and after the 63rd day—thirteen days after operation—is so very erratic that the showing made fails to indicate any adequate response to the maze environment. On the 50th day when the animals were returned to the maze the time was slightly less (90 seconds) than on the trial 3 (92 seconds) of the normal period (table 6a). Each day following the animals lost more and more time instead of gaining as they did during the normal period. The general trend of operated animals is largely established on the 52nd day.

Effect of extirpation at different ages

Extirpation at 21 days

Experiment started with 12 normal animals 21 days of age. Thyroidectomy at 21 days.

	days
Recuperation period	22 to 30
Maze learning	31 to 40
Rest period	41 to 50
Maze learning	51 to 60
Rest period	61 to 65
Maze learning	66 to 75

The twelve animals operated at 21 days of age and treated as indicated above gave a very different reaction from that of the normal control animals represented in graphs 5a, b, c, as will be seen by comparing them with graphs 7a, b, c, figure 5.

After the operation, and the ten-day recuperation period the animals were started in the maze on the 31st day for a ten-day period. Results are shown in table 7a.

Some of the animals remained in the entrance box, others moved slowly about, but did not go as far as the entrance to the

first blind alley. These animals were taken out of the maze after 30 minutes (1800 seconds) and a value of 2000 seconds assigned in computing their average performance time. The

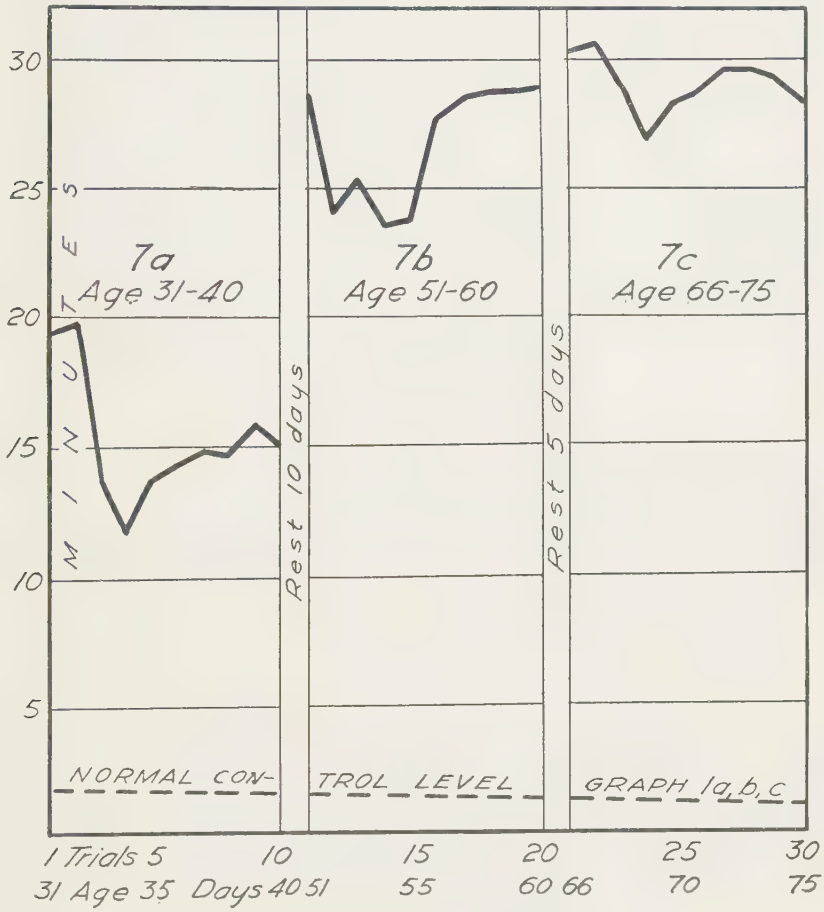

Fig. 5. Graphic Representation of Tables 7a, b, c

movements of these animals were meaningless and slow with many errors in choice of paths.

There was no evidence of learning during the ten days training. Arrival at the food box resulted from purely random wandering about if there were any movements at all. On each day of

training in the maze one or more animals did not attempt to run the maze. There was a decrease in time from the first to the tenth day by some of the animals and the average time for the group on the tenth day is less than on the first, but there is considerable fluctuation between these days. When the time

TABLE 7a

	AGE									
	31	32	33	34	35	36	37	38	39	40
Trial	1	2	3	4	5	6	7	8	9	10
Average time	1,151	1,173	834	701	835	847	898	880	948	900
Average time	19.1	19.5	13.9	11.6	13.9	14.1	14.9	14.6	15.8	15

Average of 10 trials { 917 seconds. / 15.2 minutes.

TABLE 7b

	AGE									
	51	52	53	54	55	56	57	58	59	60
Trial	11	12	13	14	15	16	17	18	19	20
Average time	1,725	1,442	1,533	1,400	1,418	1,667	1,700	1,683	1,683	1,725
Average time	28.7	24.0	25.5	23.3	23.8	27.7	28.3	28.5	28.5	28.7

Average of 10 trials { 1598 seconds. / 27 minutes.

TABLE 7c

	AGE									
	66	67	68	69	70	71	72	73	74	75
Trial	21	22	23	24	25	26	27	28	29	30
Average time	1,808	1,833	1,742	1,600	1,692	1,733	1,767	1,775	1,750	1,700
Average time	30.1	30.5	2900	26.6	28.2	28.8	29.4	29.5	29.1	28.3

Average of 10 trials { 1670 seconds. / 28 minutes.

which this group spent in the maze during this period is compared with that spent during two ten day periods following it will be seen that there is no evidence of ability to learn the maze. Table 7b gives the time in the maze following a ten-day rest interval.

The average time in the maze for the ten trials as increased from 15.2 minutes to 27 minutes.

Following this training period the rats were given another, but shorter rest period of five days. Table 7c shows their average performance during a third training period.

The average time for the ten trials increased from 27 to 28 minutes which represents practically no change.

If these tables 7a, b, c, are compared with the control tables 5a, b, c, it seems evident that after complete thyroidectomy the animals made no effective response to the maze problem.

Graphs 7a, b, c, which follow show this more clearly. The curve of activity is irregular and shows neither constant increase or decrease. The time before thyroidectomy was so short that a ten-day normal learning period could not be interpolated. For comparison the control series is roughly indicated by a dotted line. The curves of the thyroidectomized animals show only irregularities with a gradual loss of skill.

Extirpation at 37 days

Experiment started with ten normal animals 27 days of age.

	days
Normal learning period	27 to 36
Thyroidectomy	37th
Convalescence	37 to 41
Maze learning	42 to 51
Rest period	52 to 61
Maze learning	62 to 71

In this series it was possible to train the animals ten days before the operation and thus check the normal condition directly against the operated results.

The group of ten animals was started on maze training on the 27th day and learned it in the same manner as the normal (5a, b, c) control series. Table 8a is the record of their normal training period.

The average time was 89 seconds on the first day. This gradually decreased to the 60-second minimum on the eighth day. The average time of 73 seconds for the ten trials is what would be expected from normal animals.

On the the 37th day these animals were thyroidectomized

and were allowed five days instead of the usual ten days for recuperation. When returned to the maze they were forty-two days old. Table 8b gives their average performance time during the ten days (41 to 51) training period which followed.

From the table it will be seen that the average time on the 11th trial is 1094 seconds while on the 20th trial, it was 695

TABLE 8a

	AGE									
	27	28	29	30	31	32	33	34	35	36
Trial	1	2	3	4	5	6	7	8	9	10
Average time	89	86	85	78	75	70	62	60	60	60

Average of 10 trials, 73 seconds.

TABLE 8b

	AGE									
	42	43	44	45	46	47	48	49	50	51
Trial	11	12	13	14	15	16	17	18	19	20
Average time	1,094	746	1,175	740	604	404	420	447	1,319	695
Average time	18.3	12.4	19.5	12.3	10.2	6.7	7.0	7.4	21.9	28.2

Average of 10 trials { 765 seconds. / 13 minutes.

TABLE 8c

	AGE									
	62	63	64	65	66	67	68	69	70	71
Trial	21	22	23	24	25	26	27	28	29	30
Average time	2,000	1,900	1,740	1,820	1,880	1,800	1,710	1,750	1,940	1,740
Average time	33.3	31.6	29.0	30.3	31.3	30.0	28.5	29.1	32.3	29.0

Average of 10 trials { 1828 seconds. / 30 minutes.

seconds. This might be regarded as some evidence of learning ability but when the average on the 13th trial is 1175 seconds and on the 19th trial 1290 seconds, it appears that there is no regularity in performance. The maze running time is not decreased as in normal animals but shows a rapid increase and great irregularity during the ten days (42 to 51) in the maze.

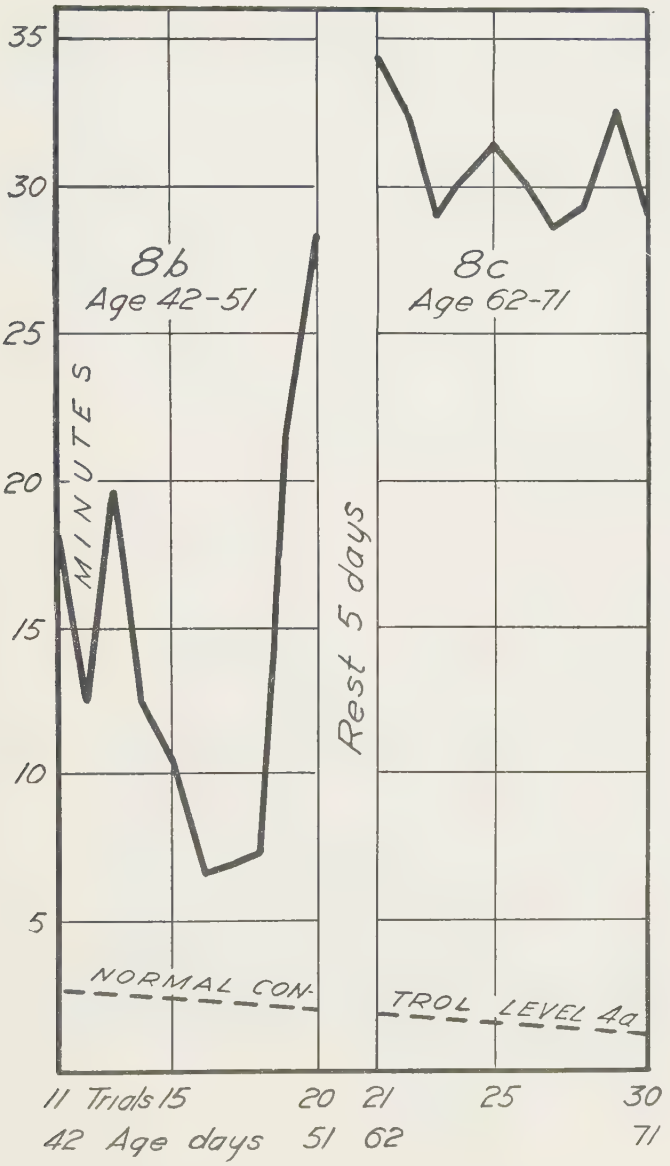

Fig. 6. Graphic Representation of Tables 8b, c

The movements are very slow and meaningless. Deterioration had reached an extent that at times, when part way through the maze, the rats would crouch down and remain there for several minutes. This might occur when the animals were practically at the entrance to the food box, within three or four steps of their food. When they moved again it was often away from the food. This would indicate that their sensitivity was dull, and the presence of food did not seem to be a stimulus to activity. The vitality of the animals was low and a constant deterioration was in evidence.

The time for the second ten-day period (62 to 71) increased rather steadily as is shown by table 8c which shows an average of 30 minutes for trials 21 to 30, as compared with 13 minutes for trials 11 to 20 in table 8b.

The irregularity of this group is better shown on graphs 8a, b, c, figure 6.

The curve for the normal period (before thyroidectomy) is only roughly indicated as a level, toward the lower part of the graph. The details may be derived from table 8a. Under normal conditions the maze time rapidly reached one minute while after the operation the average time for the group was never less than 6 minutes and nearly reached the complete failure, or 34 minute mark, on the 62nd day (graph 8c).

Worthy of particular notice is the rapid increase from 7 minutes on the 49th day to 28 minutes on the 50th. This increase in time was brought about because of the extreme slowness of the animals. The movements were meaningless, full of errors and unstable. The vitality was weak and the sensitivity was dull. The animals were unable to follow out a path without stopping two or three times and crouching near the wall of the maze. The whole behavior repertory of the rats showed great deterioration after the thyroidectomy.

Extirpation at 160 days

Experiment started with 15 normal adult animals, 160 days old. Maze learned previous to operation.

	days
Thyroidectomy	160th
Convalescence	160 to 164
Maze learning	164 to 174
Rest interval	175 to 184
Maze learning	185 to 194

A group of 15 adult animals from the stock used for breeding had been trained in the maze until they were able to run it in 60 seconds. They were given regular ten-day training periods at frequent intervals but no detailed record was kept of their activity in the maze except to check them each time to be sure

TABLE 9a

	AGE									
	165	166	167	168	169	170	171	172	173	174
Trial	1	2	3	4	5	6	7	8	9	10
Average time	81	77	77	72	82	87	98	114	126	148

Average of 10 trials, 98 seconds.

TABLE 9b

	AGE									
	185	186	187	188	189	190	191	192	193	194
Trial	11	12	13	14	15	16	17	18	19	20
Average time	159	165	180	188	194	202	212	218	228	234

Average of 10 trials, 198 seconds.

that they could run the true path in 60 seconds. They were given no practice in the maze five days before thyroidectomy.

The animals were operated upon when 160 days old, and were allowed five days for recovery. During this five-day period their general behavior was not noticeably affected. They moved about their cages as usual and did not refuse their regular ration of food.

When put into the maze on the 165th day the average time for the group was 81 seconds. The record of this period is given in table 9a.

The time decreased gradually to the 169th day and then increased during the rest of the period, the average time for

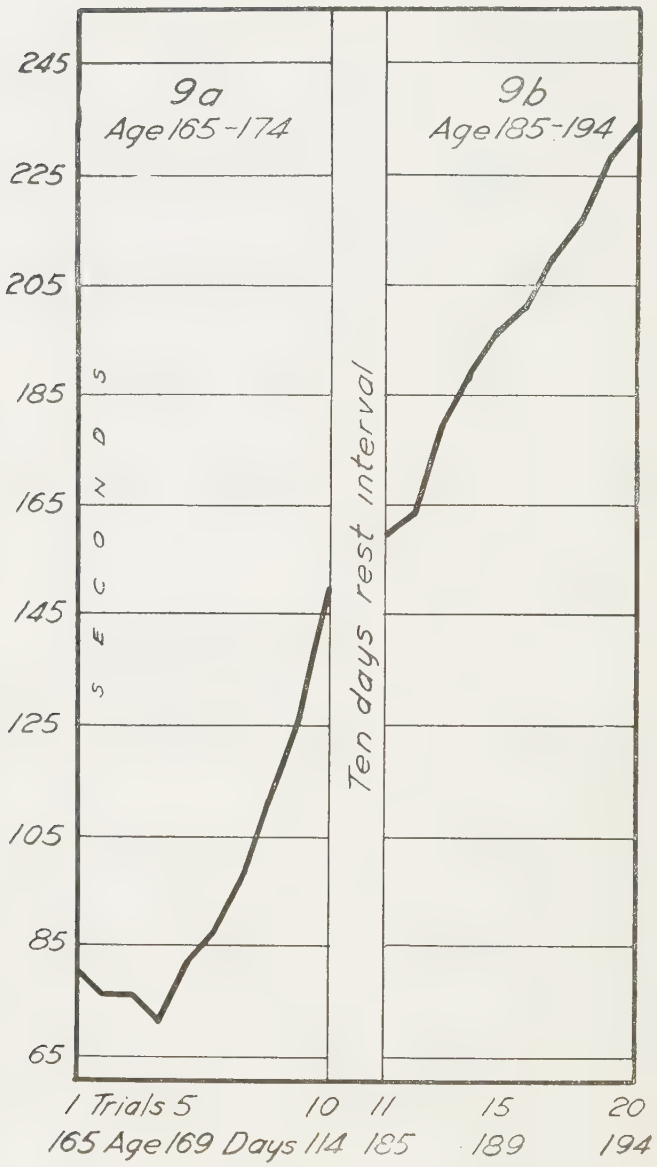

Fig. 7. Graphic Representation of Tables 9a, b, c

the period being 98 seconds, an increase of 38 seconds over normal time of 60 seconds.

A rest interval of ten days was given (174 to 184) and when the animals were returned to the maze on the 185th day the average time for the group was as given in table 9b.

Beginning with the 185th day the time spent gradually increased to the 194th day after which time no further maze training was given. The movements of these animals following the operation were not slowed up to any great extent, yet a reduced activity and dullness of sensitivity were distinctly noticeable.

The chief characteristic of this group is the steadily increasing time needed to run the maze from day to day as is shown clearly on graphs 9a, b, figure 7. There were no great fluctuations as in the case of other groups of animals which had been operated when younger.

2. Effects of extirpating thyroid in parents on learning of offspring

Since thyroidectomized males showed no sex activity, normal males from the breeding stock were mated with the thyroidectomized females. From such a mating 15 offspring were produced. The offspring were small in size, both in body length and in body weight. Most of the animals were from one-third to one-half smaller than normal animals of the same age. All movements were slow; and lethargy and general malaise were common, with troubles of locomotion and vasomotor disturbances. The offspring were trained in the maze during the ten-day period 36 to 45 days.[2] Table 10a shows the results during the training period.

Their activity was so limited, their movements so slow and their vitality so weak that the results can hardly be regarded as showing any ability to learn. When the animals do find their way in the center (81 out of 150 trials) this seems to be a matter

[2] At the end of the training 36 to 45 days, this group was given no further maze training, but the females were bred with normal males for a second generation from operated animals.

of chance. Graph 10a shows more clearly the tendency of this group to random movement.

A second group of thyroidectomized females were bred to normal breeding stock males and produced eighteen offspring which were physically of about the same type as those obtained in the group whose activities are reported in table 10a.

TABLE 10a

	AGE									
	36	37	38	39	40	41	42	43	44	45
Trial	1	2	3	4	5	6	7	8	9	10
Average time in minutes	33	28	30	30	30	29	30	30	30	29

Average of 10 trials, 30 minutes.

TABLE 10b

	AGE									
	36	37	38	39	40	41	42	43	44	45
Trial	1	2	3	4	5	6	7	8	9	10
Average time (minutes)	33	26	30	28	29	28	30	28	30	28

Average of 10 trials, 25 minutes.

TABLE 10c

	AGE									
	56	57	58	59	60	61	62	63	64	65
Trial	11	12	13	14	15	16	17	18	19	20
Average time	4	3	3	3	2	2	2	2	1.9	1.8

Average of 10 trials, 2.8 minutes.

These offspring were trained in the maze during the 36 to 45 day period. From 46 to 55 days was a rest period during which 0.30 gram T. G. S. was fed daily.

Maze training occured during the 56 to 65 day period, while the 0.30 gram T. G. S. daily feeding continued, table 10b shows the maze record before T. G. S. feeding.

The average time for the ten trials of this untreated group (25 minutes) is somewhat faster than the average (30 minutes) of the untreated groups shown in table 10a.

The effect of the T. G. S. feeding on this group is clearly shown in table 10c.

There was a very marked change in the behavior following the thyroid treatment. The movements were faster and the

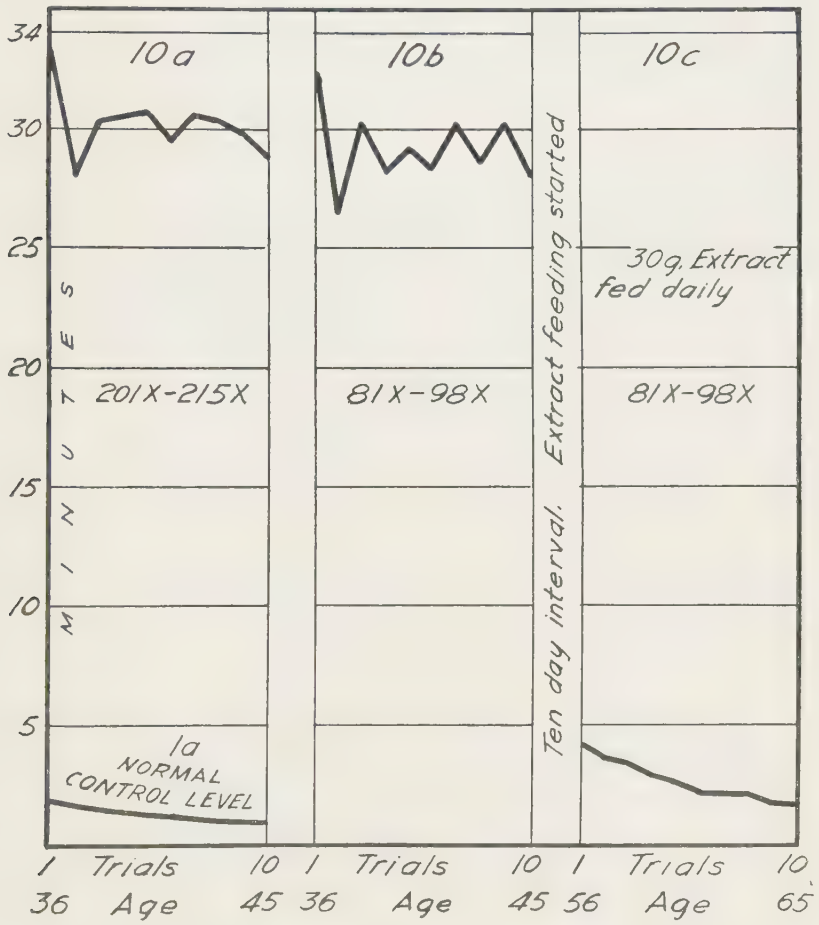

Fig. 8. Graphic Representation of Tables 10a, b, c

general behavior of the animals became nearly normal. There was a very slight increase in size following treatment. The maze was traveled in 1.8 minutes on the 20th day after feeding was started which is only 0.8 minutes longer than the time for perfectly normal animals.

The pronounced effect of the T. G. S. feeding is best indicated by reduction in maze time from about 30 minutes in 10b, to about 3 minutes in 10c. The downward slope of the learning curve is also a good indication that behavior factors are approaching normal conditions.

3. Effects of extirpation of thyroid in parents and grandparents on learning of offspring

Experiment was started with ten animals which were the offspring of operated females and normal males. The females in this experiment were the offspring of normal males and thyroidectomized females. None of the female progenitors had received any T. G. S. treatment until after breeding and gestation periods were over. The third generation offspring group were very small, most of them being about one-fourth as large as normal animals of the same age. Sensitivity was very dull and vitality extremely low. General malaise and troubles of locomotion were common. The experimental program was as follows:

	days
Maze learning	31 to 40
Maze learning (0.30 gram T. G. S. injected daily beginning on 41st day)	41 to 50
Rest intervals (0.30 gram T. G. S. injections continued)	51 to 55
Maze learning (0.30 gram T. G. S. injection continued)	56 to 65

The results without T. G. S. injection are given in table 11a. There is no evidence of ability to learn to run the maze. Sixty-six out of the one hundred opportunities were complete failures. The average time, 31 minutes, is only about two minutes less than the 34 minutes which would have indicated complete failure.

Beginning at 41 days 0.30 gram thyroid gland was injected daily into each animal of the group. After three days' treatment all animals found their way to the food box. Results of this period are given in table 11b.

Compared with the average time of 31 minutes in the preceding period without T. G. S., the 16 minutes average of the 11 to 20

trial period shows an effect due to thyroid injection which is very pronounced.

Following a rest period from 51 to 55 days, during which the T. G. S. treatment was continued, this group was returned to the maze with the results given in table 11c.

On the sixth day in the maze all animals gave a uniform performance of 120 seconds. This was continued during the four days following.

TABLE 11a

	AGE									
	31	32	33	34	35	36	37	38	39	40
Trial	1	2	3	4	5	6	7	8	9	10
Average time (minutes)	31	32	30	31	31	31	31	31	31	32

Average of 10 trials, 31 minutes.

TABLE 11b

	AGE									
	41	42	43	44	45	46	47	48	49	50
Trial	11	12	13	14	15	16	17	18	19	20
Average time (minutes)	33	30	19	16	20	17	14	9	3	2

Average of 10 trials, 16 minutes.

TABLE 11c

	AGE									
	56	57	58	59	60	61	62	63	64	65
Trial	21	22	23	24	25	26	27	28	29	30
Average time	3	2	2	2	2	2	2	2	2	2

Average of 10 trials, 2 minutes.

The general behavior was much improved after the T. G. S. treatment. The movements were faster and more stable, there was a very marked improvement in the ability to run the maze, and the average time had decreased from 16 minutes to 2 minutes. The troubles of locomotion had almost entirely disappeared. Sensitivity increased, the malaise disappeared, and the animals took on an a most normal appearance with the exception of size which continued much below normal.

Graph 11b, c, figure 9, shows the very decided drop in time spent in the maze following T. G. S. injection. Before injection (11a) there is no evidence of learning, the curve of the perform-

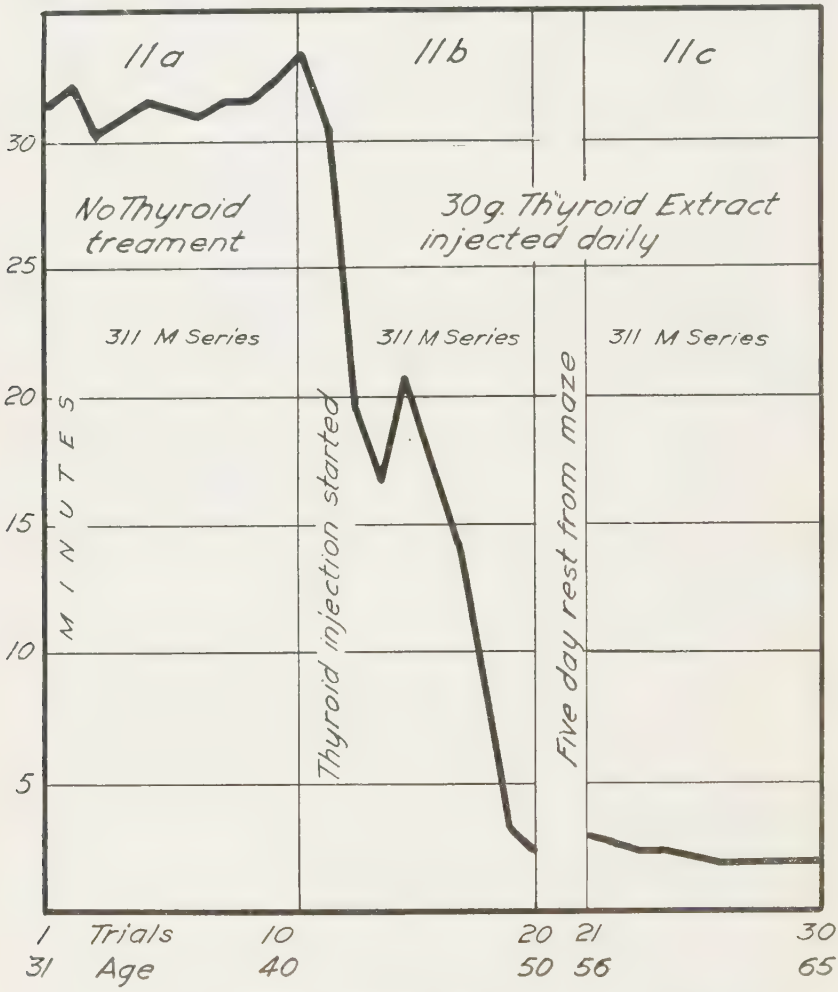

Fig. 9. Graphic Representation of Tables 11a, b, c

ance time shows no tendency toward improvement. Beginning at 41 days (11b, c) the curve steadily shows the effect of the T. G. S. injection and drops from 16 minutes to 2 minutes, which is almost the normal limit of 1 minute.

4. Summary of experiment I, extirpation of thyroid gland

1. The behavior after thyroidectomy shows a progressive incoördination, the movements becoming slower, less stable, meaningless, and whatever pre-operative learning has been acquired is lost. Vitality is reduced, sensitivity decreased, and there is a progressive deterioration of the vegetative processes. These effects are more pronounced in the younger animals. In the males sex activity disappears, but the females do not become sterile.

2. To secure the second generation, it was necessary to mate normal males with thyroidectomized females. The offspring were small, underweight, with locomotor and vaso-motor deficiencies. While the animals do find the food box and some evidence of improvement seems indicated, the level of performance (30 minutes) of the offspring seems hardly comparable with the performance level (one minute) of normal animals (graph 10a, b, fig. 8).

When the first generation offspring of thyroidectomized females are fed T. G. S. there is an immediate improvement. The lethargy and general malaise disappear and the offspring rapidly approach the behavior and vegetative conditions of normal animals.

3. The second generation offspring without T. G. S. show a degree of deterioration greater than the second generation offspring without T. G. S. But when this second generation is injected with T. G. S., they approach the normal behavior level very closely although as to size and weight they are still much below normal.

IX. EXPERIMENT II

1. Effect of injecting thyroid gland substance on learning

The purpose of this experiment will be to investigate the effects which the injection of T. G. S. has upon animals of different ages and the progeny of these animals. Animals of different ages were used in the experiment because it was found in the preliminary experiment on injection of T. G. S. that age was a

factor in determining the amount of T. G. S. which could be tolerated with the maintenance of apparently normal health. The progeny of the T. G. S. animals were given no treatment.

Normal control series

(No T. G. S. injection)

Ten normal animals 21 days old were used.

	days
Maze learning	21 to 40
Rest period	41 to 45
Maze relearning	46 to 55

This group gave results practically identical with the other series of normal rats (5a, b, c) that were used. The first ten days are shown in table 12a.

TABLE 12a

	AGE									
	21	22	23	24	25	26	27	28	29	30
Trial	1	2	3	4	5	6	7	8	9	10
Average time	114	99	99	91	81	78	70	60	60	60

Average of 10 trials, 81 seconds.

This table shows that the average time spent in the maze decreased from 2 minutes on the first day to 1 minute on the 8th day and this average remained the same on the two following days. The average time of the ten trials was 81 seconds.

The second ten day period was continuous with the period just reported and the animals continued to run the maze in average time of about one minute. Table 12b gives a condensed report of the activity of these animals.

After a five day rest period (41 to 45) the anima's again ran the maze in an average time of 69 seconds on the first day (21st day of series) and after the the first day the average remained at 60 seconds with the exception of 61 seconds on the 26th day. The results of this period of training are given in table 12c.

Graphs 12a, b, c, figure 10, show the normal behavior of these animals. The curves have a downward slope and time limits

TABLE 12b

	AGE									
	31	32	33	34	25	36	37	38	39	40
Trial	11	12	13	14	15	16	17	18	19	20
Average time	63	63	61	63	60	60	60	60	60	60

Average of 10 trials, 61 seconds.

TABLE 12c

	AGE									
	46	47	48	49	50	51	52	53	54	55
Trial	21	22	23	24	25	26	27	28	29	30
Average time	69	60	60	60	60	61	60	61	60	60

Average of 10 trials, 61 seconds.

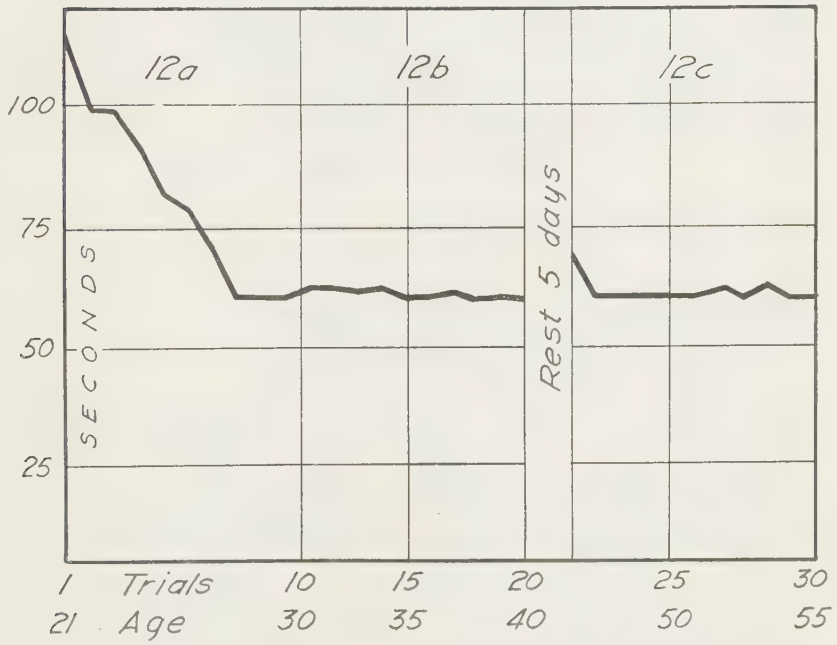

FIG. 10. GRAPHIC REPRESENTATION OF TABLES 12a, b, c

which are indicative of learning. The slight rise in the curve at the 46th day, the first day in the maze after a five day rest period, is negligible.

a. Effect of injection at different ages

Animals of different ages were used in the learning experiment, as it was determined in the preliminary toleration experiment that the amount of T. G. S. tolerated varied with age. This was also the reason for increasing dosage with increase of age; because it was desired to give the animals as much as could be tolerated with apparently normal health in order that the effect of this tolerated amount of T. G. S. on learning ability might be found.

The desiccated gland was mixed with water and injected directly into the blood stream by way of the femoral artery. The substance was placed in a small hyperdermic syringe and the injection was made where the artery runs close to the skin on the under side of the hind leg. The amount given by this method was about one-half of the amount given when the animals were allowed to eat the T. G. S. mixed with milk.

Injection at 21 days

Ten normal animals were used.

	days
Maze learning (0.15 gram T. G. S. injected daily)	21 to 30
Maze learning (0.25 gram T. G. S. injected daily)	31 to 40
Rest interval (0.25 gram T. G. S. injected daily)	41 to 45
Maze learning (0.30 gram T. G. S. injected daily)	46 to 55

The results of the first ten trials in the maze with injection of 0.15 gram T. G. S. daily are shown in table 13a.

The average time, 119 seconds, spent in the maze by these animals on the first day is five seconds longer than that spent by normal rats (table 12a) but on the second day when the normal animals decrease to 99 seconds the injected animals show the same performance as on the first day. The third day resulted in a considerable increase in time for this group and from that day on the time which they take to travel the maze increases.

Comparing the averages for the ten day periods, the normal rats show 81 seconds, the injected 153 seconds.

Continuing to the second ten day training period which followed directly with no interval for rest we find the same fact holding true. The animals have no ability to learn the maze and do not even hold to the time made during the first ten days as is shown in table 13b which follows.

TABLE 13a

	AGE									
	21	22	23	24	25	26	27	28	29	30
Trial	1	2	3	4	5	6	7	8	9	10
Average time	119	119	134	152	150	175	162	117	162	180

Average of 10 trials, 153 seconds.

TABLE 13b

	AGE									
	31	32	33	34	35	36	37	38	39	40
Trial	11	12	13	14	15	16	17	18	19	20
Average time	221	266	270	325	330	390	397	480	410	382

Average of 10 trials, 325 seconds.

TABLE 13c

	AGE									
	46	47	48	49	50	51	52	53	54	55
Trial	21	22	23	24	25	26	27	28	29	30
Average time	385	400	450	455	400	450	500	500	400	500

Average of 10 trials, 440 seconds.

The time increases steadily through this period from 221 to 382 seconds. This increase varies greatly from the normal behavior in which there is a regular decrease from day to day. The average time for the corresponding ten day periods are; 61 seconds for the normal, and 325 seconds for the injected animals.

After a five day rest interval during which the amount of

T. G. S. was increased to 0.30 gram daily the animals were returned to the maze with the results given in table 13c.

The most noticeable item in the performance during this period is the irregularity in behavior. The variability from day to day is not due to slow movement but to a swift and meaningless jumping about with no attempt to correct previous errors and profit by former experiences in the maze. The rats are very irritable and excitable and show a super-activity at all times both in

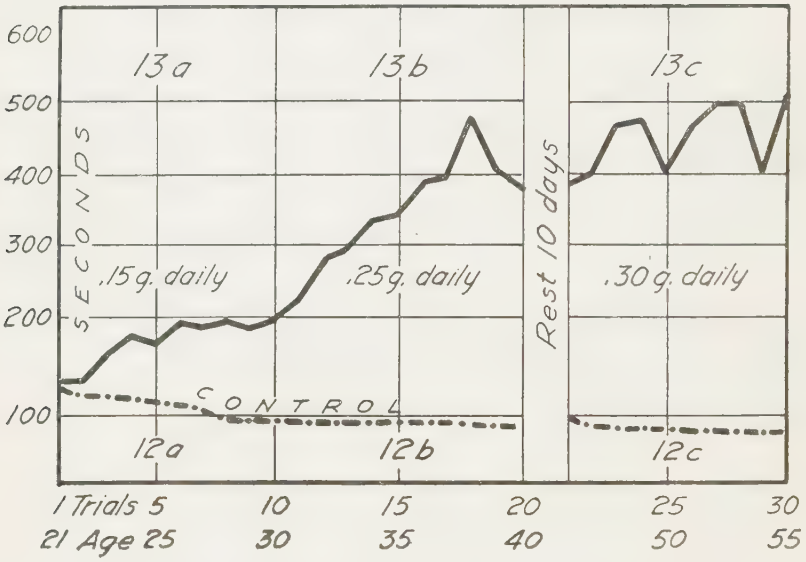

Fig. 11. Graphic Representation of Tables 13a, b, c

the maze performances and in their home cages. The average of 325 seconds for trials 11 to 20 is lengthened to 440 seconds in trials 21 to 30, although the animals are more active in the latter period.

Graph 13a, b, c, figure 11, shows the tendency of the group toward an increased maze time to a certain point, about 400 seconds, and after this there is an increase and decrease of the maze running time with no apparent regularity for the ten day period.

Injection at 36 days

Ten animals were used.

	days
Maze learning (0.15 gram T. G. S. injected daily)	36 to 45
Maze learning (0.25 gram T. G. S. injected daily)	46 to 55
Rest interval (0.25 gram T. G. S. injected daily)	56 to 60
Maze learning (0.30 gram T. G. S. injected daily)	61 to 70

The animals were started on maze training and T. G. S. injection on the same day. The amount of T. G. S. was increased as shown so as to overcome the effects of adaptation and because it was found that the older the animal became the more T. G. S. he could tolerate. Table 14a shows the average performance time of the group for the first ten-day period.

TABLE 14a

	AGE									
	36	37	38	39	40	41	42	43	44	45
Trial	1	2	3	4	5	6	7	8	9	10
Average time	108	114	115	122	134	136	144	144	136	134

Average of 10 trials, 129 seconds.

The average time for the first day is six seconds less than that required by the normal animals reported in table 12a. After the first day there is a gradual rise in the time which is spent in the maze, which continues through the whole ten-day training.

Training was continued with no rest interval but on the 45th day the amount of T. G. S. injected was increased to 0.25 gram. Table 14b gives the average of this stage of their training.

During this period of training, the animals were very excitable and nervous and the high average performance time of 335 as compared with 129 seconds, is caused by a hyperactivity which is meaningless and unstable.

Beginning on the 55th day the rats were given a five day rest interval from the maze, but the daily T. G. S. injection continued. On the 61st day the amount given was increased to 0.30 gram, and continued during the period of 61 to 70 days which the animal spent in the maze. Table 14c gives the maze running results.

TABLE 14b

	AGE									
	46	47	48	49	50	51	52	53	54	55
Trial	11	12	13	14	15	16	17	18	19	20
Average time	305	290	330	300	360	345	366	350	350	350

Average of 10 trials, 335 seconds.

TABLE 14c

	AGE									
	61	62	63	64	65	66	67	68	69	70
Trial	21	22	23	24	25	26	27	28	29	30
Average time	456	460	510	500	505	495	490	495	490	475

Average of 10 trials, 488 seconds

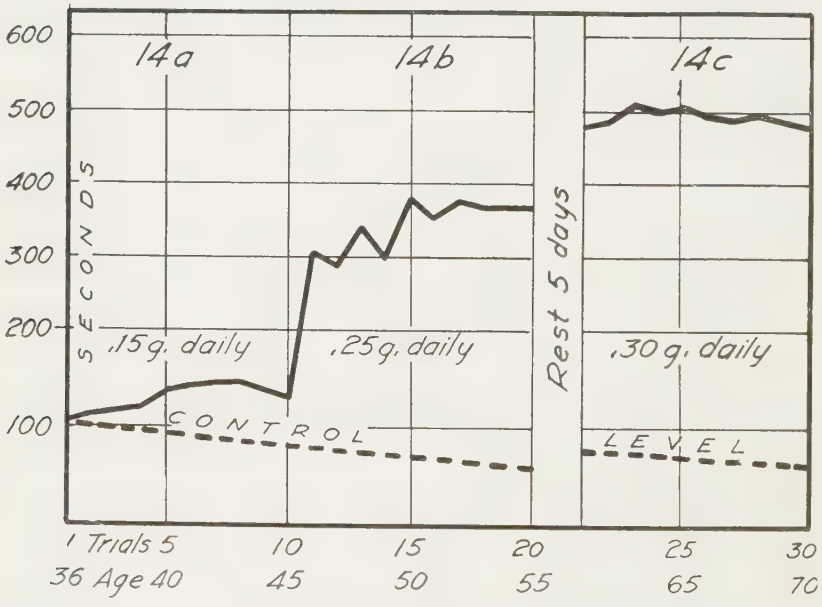

Fig. 12. Graphic Representation of Tables 14a, b, c

The activity of these animals in the maze is similar to that of the 21-day group of injected animals reported in tables 13a, b, c. There is a regular rise in time during the first period of training up to about 400 seconds after which the animals neither increase greatly nor show any evidence of learning.

Graph 14a, b, c, figure 12, represents the activity of the rats during the 30 days of work in the maze. The similarity of the behavior between the 21-day and 36-day groups becomes apparent when graph 13a, b, c, is compared with 14a, b, c, and the effect of the T. G. S. injection is clearly brought out when the graphs are compared with the normal control series 12a, b, c, indicated on both graphs.

Injection at 155 days

Thirty-five animals were used.

	days
T. G. S. injection (0.35 gram daily)	155 to 160
Maze learning (0.40 gram injected daily)	160 to 169

Thirty-five adult animals which were able to run the maze in 60 seconds were selected. These rats were trained at different times, and no detailed record was kept of their work except to note that their behavior was normal. They were given no opportunity to run the maze for the ten days preceding the beginning of the T. G. S. injection.

Beginning at 155 days of age the animals were injected with 0.35 gram T. G. S. daily; at 160 days the amount was increased to 0.40 gram and the animals started in the maze. Table 15 is a record of their activity for the ten day period during T. G. S. treatment.

The time is seen to increase gradually, but only to a very small amount, the rat's behavior was stable in most cases with a slight tendency for the rat to become excited and nervous when in the maze. In the home cages the animals appeared perfectly normal.

Graph 15, figure 13, gives a picture of their maze running, and the rise in the curve is very slight as may be seen from the

TABLE 15

	AGE									
	160	161	162	163	164	165	166	167	168	169
Trial	1	2	3	4	5	6	7	8	9	10
Average time	68	67	77	81	85	88	92	96	105	108

Average of 10 trials, 87 seconds.

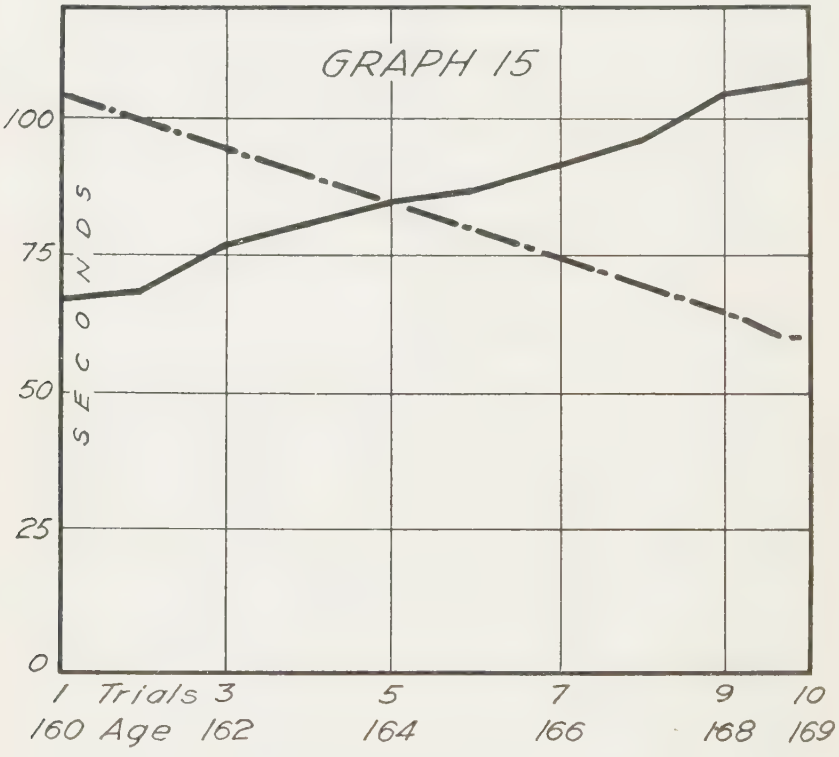

FIG. 13. GRAPHIC REPRESENTATION OF TABLE 15

normal level which is placed on the same graph. However, the deteriorating effect on the behavior is evident since the animals are not able to maintain the normal level when T. G. S. is injected. There is some indication that the effect of T. G. S. becomes less with age.

b. Effect on learning of offspring when parents were injected with T. G. S.

First generation offspring

Animals which were bred after the T. G. S. treatment produced 14 offspring. These animals were slightly smaller than normal, and the only striking feature in their appearance was the protruding eyeball. They were less normal in their movements about the home cages than the offspring of normal animals. They had a tendency to jump violently and quickly away from the door of the cage when it was opened. These quick, jerky

TABLE 16a

	AGE									
	25	26	27	28	29	30	31	32	33	34
Trial	1	2	3	4	5	6	7	8	9	10
Average time	116	118	121	120	118	122	126	123	121	122

Average of 10 trials, 121 seconds.

TABLE 16b

	AGE									
	35	36	37	38	39	40	41	42	43	44
Trial	11	12	13	14	15	16	17	18	19	20
Average time	113	117	127	127	132	126	124	121	126	130

Average of 10 trials, 124 seconds.

movements were very common both in the home cage and in the maze. The experimental program was as follows:

Fourteen animals were used.

	days
Maze learning (no T. G. S. treatment)	25 to 44

At the age of 25 days these animals were placed in the maze for a training period of 20 days. The results are given in tables 16a, b.

These results show that the animals did not reach the 60-second minimum and remained at practically the same level as the normal rats on their first trial. These animals were given

no thyroid extract so that whatever weakness they show in ability to learn may be due to the excess thyroid which was given to the parents. The curve of their behavior shown in graph 16a, b, figure 14, indicates the irregularity of their maze performance. The curve slopes upward rather than downward and the time is double that of normal animals.

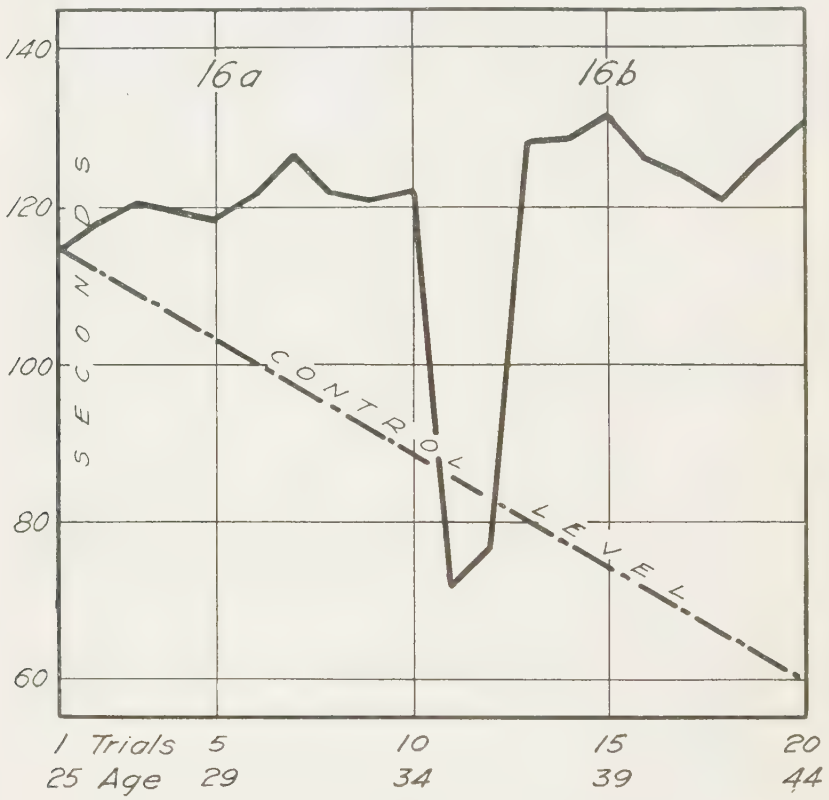

Fig. 14. Graphic Representation of Tables 16a, b

Second generation offspring

Fifteen animals which were second generation offspring of injected animals were used in this part of the study. The experimental program for this group was as follows:

	days
Maze learning (no T. G. S. treatment)	31 to 50

The results of the training of this group during a 20-day period are given in tables 17a, b.

The long time which these rats spent in the maze seems to be due to extreme hyperactivity. Their reactions were very unstable, nervous and meaningless. One fact to be noticed is that even though the time is great for each animal, there is no day in the series on which any animal fails completely to find the center and the food box.

Graph 17a, b, figure 15, shows that there is some evidence that the time in the maze was decreasing, although the absolute time,

TABLE 17a

	AGE									
	31	32	33	34	35	36	37	38	39	40
Trial	1	2	3	4	5	6	7	8	9	10
Average time	26	24	24	23	22	21	21	21	19	16

Average of 10 trials, 22 minutes.

TABLE 17b

	AGE									
	41	42	43	44	45	46	47	48	49	50
Trial	11	12	13	14	15	16	17	18	19	20
Average time	17	16	17	16	16	18	16	15	17	18

Average of 10 trials, 17 minutes.

and the fact that the experimental period is for only twenty days does not justify any definite conclusions.

2. Summary of experiment II, effect of injecting thyroid gland substance

1. The effect of the T. G. S. on learning is practically to eliminate it. There gradually develops a swift and meaningless jumping about and, instead of a dropping off of useless movements, the number of errors actually increases. The instability and hyperactivity increase both in the maze and in the home cages, but the effect of the T. G. S. injections seems to decrease with age.

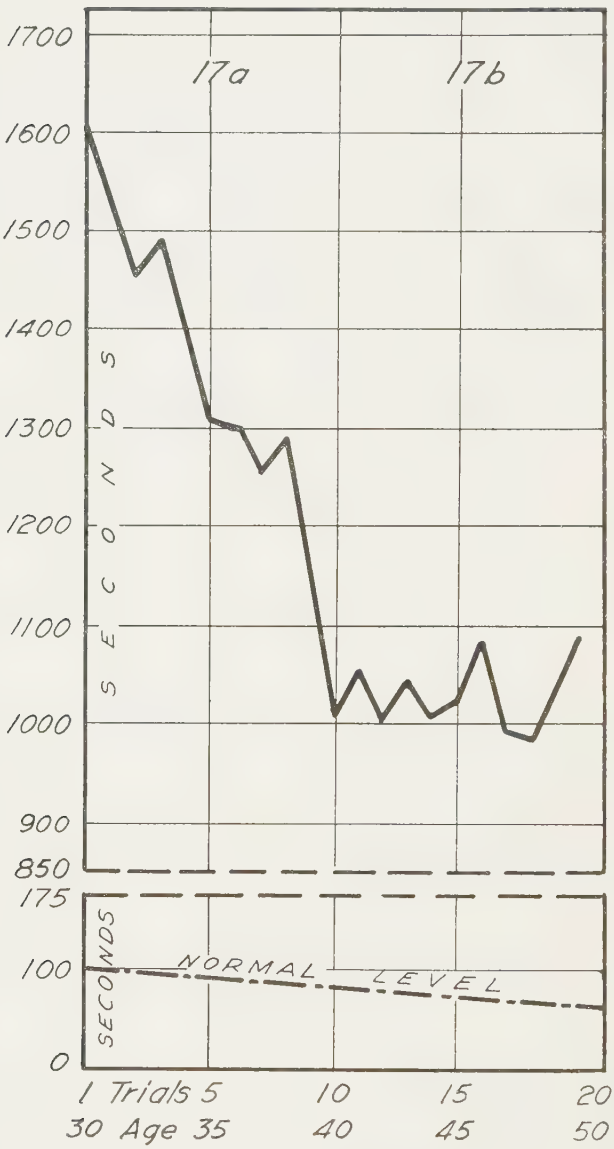

Fig. 15. Graphic Representation of Tables 17a, b

2. The offspring of parents which had been injected with T. G. S. were slightly smaller than normal and had protruding eyeballs. Their movements were jerky. Their maze record was about the same as that of normal rats at the beginning, but showed no improvement during the short time they served in the experiment.

3. The second generation of offspring from parents and grandparents which had been injected with T. G. S. were extremely active, unstable and nervous. While there is some evidence of learning in the maze record, the experimental period is too short to justify any conclusion.

X. EXPERIMENT III

1. Effect on learning of feeding T. G. S. to normal animals

This experiment will be concerned with the effects on learning which follow the feeding by mouth of varying amounts of T. G. S. in animals of different ages and their offspring. The preliminary toleration experiment, in which learning was not considered, seemed to show that the amount of T. G. S. which could be tolerated varied with age, the older animals taking more of the T. G. S. with apparent maintenance of good health than the younger. The progeny of the "fed" animals were given no treatment with T. G. S. The desiccated T. G. S. was mixed with milk and fed to the animals just before the regular ration of food in the morning. The animals ate all of the mixture given each time. The amount given in this way was about twice the amount given by injection. The training in the maze and the T. G. S. feeding were begun at the same time.

a. Feeding T. G. S. at different ages

Series at 21 days

The animals were selected at weaning time (21 days) and started on the maze, at the same time being fed 0.30 gram T. G. S. daily for ten days in conformity with the following experimental program:

Ten animals were used.

	days
Maze learning (0.30 gram T. G. S. fed daily)	21 to 30
Maze learning (0.35 gram T. G. S. fed daily)	31 to 40
Rest period (0.35 gram T. G. S. fed daily)	41 to 45
Maze learning (0.35 gram T. G. S. fed daily)	46 to 55

Table 18a which follows gives the results for the first maze learning period.

The results show a gradual increase in time from day to day, instead of a rapid drop for the first days which is characteristic of normal animals. The animals were very much excited when placed in the maze and seemed frightened. Their movements

TABLE 18a

	AGE									
	21	22	23	24	25	26	27	28	29	30
Trial	1	2	3	4	5	6	7	8	9	10
Average time	125	124	144	160	174	188	176	186	194	220

Average of 10 trials, 170 seconds.

TABLE 18b

	AGE									
	31	32	33	34	35	36	37	38	39	40
Trial	11	12	13	14	15	16	17	18	19	20
Average time	241	320	325	365	358	425	446	510	505	512

Average of 10 trials, 450 seconds.

were quick and meaningless, and they gave the same sort of unstable behavior each day.

On the 31st day the amount given was increased to 0.35 gram; the maze training was continued without a break. The results are shown in table 18b.

The behavior of the animals was increasingly unstable during this period. They would run in one direction rapidly, turn squarely around and run in the opposite direction. This sort of behavior would continue for some time. In the face of this greater activity, the maze time for the group increased from 170 second for the first ten trials (1 to 10) to 450 seconds for trials 11 to 20.

TABLE 18c

	AGE									
	46	47	48	49	50	51	52	53	54	55
Trial	21	22	23	24	25	26	27	28	29	30
Average time	514	515	567	602	670	670	725	710	718	763

Average of 10 trials, 645 seconds.

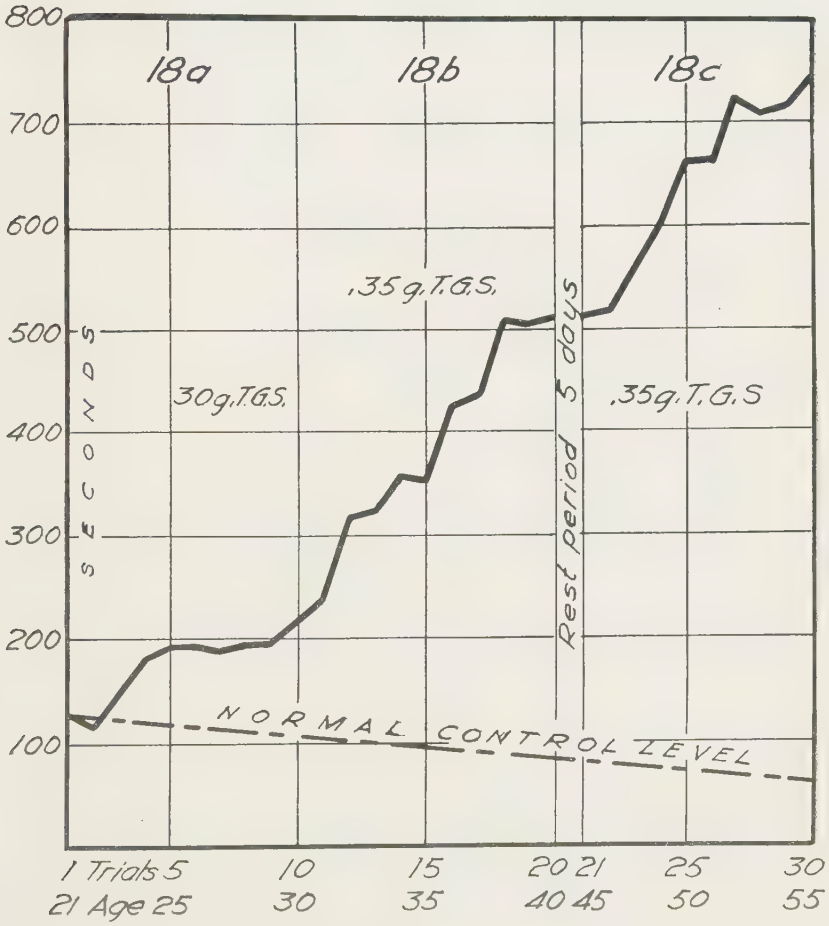

FIG. 16. GRAPHIC REPRESENTATION OF TABLES 18a, b, c

The same dosage (0.35 gram) was continued through a five day rest period, and at 46 days of age the animals were returned to the maze while the T. G. S. feeding continued. Table 18c gives the result of the third ten days training period.

The instability of the animals increased; the movements continued to be meaningless; and the sensitivity seemed greatly impaired as the animals would run into the walls of the maze time after time before continuing the path of the maze. It is to be noticed especially that even though the movements are erratic and unstable all animals successfully reach the food box every trial.

Graph 18a, b, c, figure 16, shows how constantly the maze running time of this group increased. In order to show the effect of the T. G. S. feeding a normal level is added for comparison.

Series at 36 days

Ten normal animals were used.

	days
Maze learning (0.40 gram T. G. S. fed daily)	36 to 45
Maze learning (0.45 gram T. G. S. fed daily)	46 to 55
Rest period (0.45 gram T. G. S. fed daily)	55 to 60
Maze learning (0.45 gram T. G. S. fed daily)	61 to 70

The group was fed 0.40 gram of T. G. S. beginning at 36 days of age. The training was started at the same time with the feeding. The tendency of the whole group was to increase the time from day to day, as is shown in table 19a.

Training was continued without intermission and on the 46th day the dosage was increased to 0.45 gram of T. G. S. daily. During the period 46 to 55 days the time continued to increase as shown in table 19b.

The consistent increase evident here is still to be found in the behavior of the animals after a five day rest period, during which time the T. G. S. treatment was continued. Table 19c gives the time which the animals spent in the maze after their rest period. This was the last training which the animals were given.

The consistent increase in time is further shown by the average times for the three training periods, which show 138, 394, 535 seconds for the 1st, 2nd, and 3rd periods respectively.

Graph 19a, b, c, figure 17, gives a continuous picture of the activity of the animals and the gradual rise in time to the 55th day. After that day the average time varies a great deal but shows a tendency to increase slightly to the end.

TABLE 19a

	AGE									
	36	37	38	39	40	41	42	43	44	45
Trial	1	2	3	4	5	6	7	8	9	10
Average time	114	118	118	128	135	140	148	154	157	162

Average of 10 trials, 138 seconds.

TABLE 19b

	AGE									
	46	47	48	49	50	51	52	53	54	55
Trial	11	12	13	14	15	16	17	18	29	20
Average time	298	283	325	360	375	406	437	455	491	505

Average of 10 trials, 394 seconds.

TABLE 19c

	AGE									
	61	62	63	64	65	66	67	68	69	70
Trial	21	22	23	24	25	26	27	28	29	30
Average time	495	531	523	501	525	583	557	583	562	535

Average of 10 trials, 535 seconds.

Series at 155 days

Thirty-five normal animals were used.

	days
0.70 gram T. G. S. fed daily	155 to 160
Maze learning (0.70 gram T. G. S. fed daily)	160 to 169

Thirty-five normal adult animals which had learned the maze at various intervals during their life time were selected for this experiment. Beginning at 155 days the animals were given 0.70 gram T. G. S. mixed with milk each day. This treatment was

continued for five days and at 160 days of age all the animals were started in the maze together. The treatment was continued during the time of training. These animals were given only one ten day training period for the reason that the time which they spent in the maze increased so rapidly and their behavior was so similar to that of other treated animals that further training was

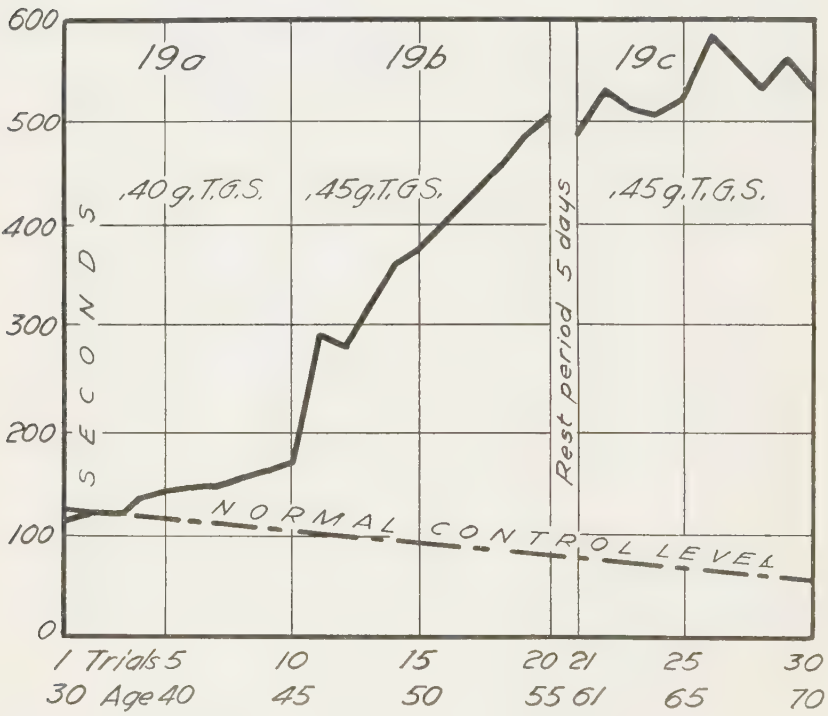

Fig. 17. Graphic Representation of Tables 19a, b, c

considered unnecessary. Table 20 gives the average time during the ten day period.

Graph 20, figure 18, shows the curve of the time spent in the maze by the group and the gradual increase is to be noted here. There is also included on this the level of the normal control group 5c for the third maze learning period, which is comparable with the experimental series which had already learned the maze before.

b. Effect on learning of offspring of T. G. S. fed parents

The animals which had been fed T. G. S. were bred. The treatment of feeding 0.70 gram of T. G. S. daily was continued during the period of gestation. Three litters of four, six, and four, animals respectively were obtained and the appearance of the animals was normal in every respect. These offspring were

TABLE 20

	AGE									
	160	161	162	163	164	165	166	167	168	169
Trial	1	2	3	4	5	6	7	8	9	10
Average time	71	77	81	83	94	104	103	109	114	115

Average of 10 trials, 95 seconds.

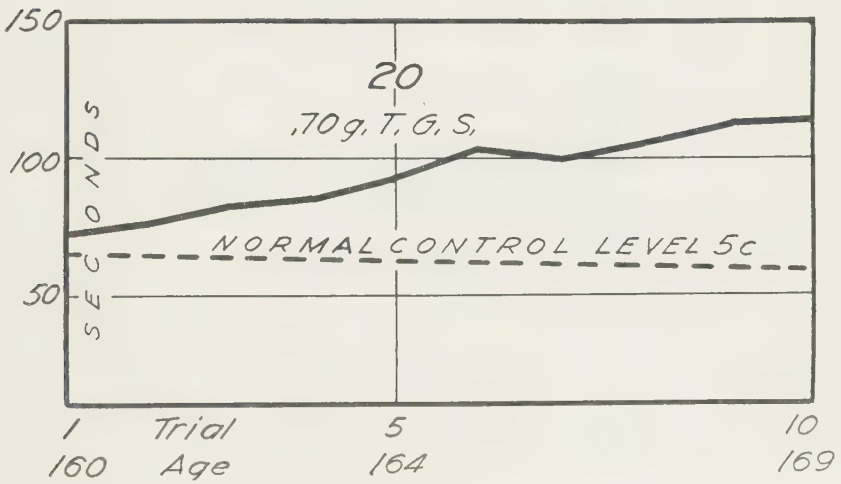

FIG. 18. GRAPHIC REPRESENTATION OF TABLE 20

not given treatment with T. G. S., but were started in the maze at 25 days of age with no further experimental variation of the thyroid conditions during their period of thirty days training in the maze. The experimental program was as follows:

Fourteen animals (offspring of T. G. S. fed animals) were used.

	days
Maze learning	25 to 44
Rest period	45 to 49
Maze learning	50 to 59

These offpsring received no T. G. S. at any time.

The results of the behavior are given in tables 21a, b, c.

The curve of these three ten-day maze periods is given in graph 21 a, b, c, figure 19. Here it may be seen that there is a

TABLE 21a

	AGE									
	25	26	27	28	29	30	31	32	33	34
Trial	1	2	3	4	5	6	7	8	9	10
Average time	95	118	130	148	141	143	148	145	148	148

Average of 10 trials, 136 seconds.

TABLE 21b

	AGE									
	35	36	37	38	39	40	41	42	43	44
Trial	11	12	13	14	15	16	17	18	19	20
Average time	138	145	150	150	165	172	172	175	177	177

Average of 10 trials, 162 seconds.

TABLE 21c

	AGE									
	50	51	52	53	54	55	56	57	58	59
Trial	21	22	23	24	25	26	27	28	29	30
Average time	138	145	160	182	168	185	180	191	182	205

Average of 10 trials, 174 seconds.

general rise in time spent in the maze up to about 40 days. The rest period which started at the 45th and continued to the 49th day seems to have had a favorable influence for a few days after the third maze period started. It lasted for only a short while and the 53rd day (table 21c) showed an average of 183 seconds which was higher than the previous maximum of 177 seconds (table 21b). Even with the apparently favorable effect of the rest period the average of 174 seconds for the ten day period after

the rest, is higher than the ten day average of 162 seconds (table 21b) before the rest.

The behavior of this group was very erratic and nervous. The rats succeeded in reaching the central box each day but only

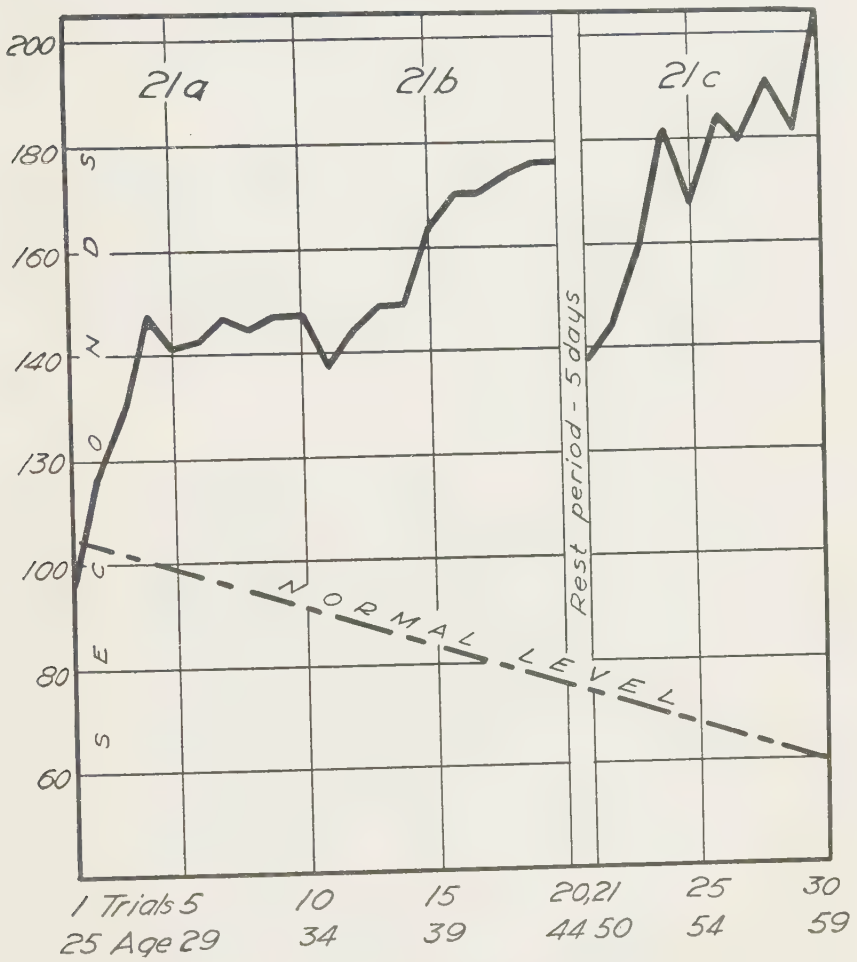

FIG. 19. GRAPHIC REPRESENTATION OF TABLES 21a, b, c

after a series of meaningless and unstable movements. Their activity about the home cages was also very erratic, they would jump, bite, and claw about the cage almost continually.

2. Summary of experiment III, effect of feeding T. G. S. to normal animals

1. In general the feeding of T. G. S. results in a loss of skill and accuracy which is proportional to the amount fed and inversely proportional to the age of the animals. The movements become more rapid but less coördinated, and the effects of previous coördination gradually vanish in erratic and convulsive forms of behavior.

2. The offspring of males and females being fed 0.70 gram T. G. S. during the period of breeding and gestation showed a very erratic and nervous behavior both around the home cages and in the maze. While the offspring themselves received no T. G. S. treatment and in appearance seemed normal, there was no evidence of learning ability in the sense that their maze records improved with repetition.

XI. FAMILY CHARTS

With the legend the charts of figure 20 are self-explanatory, but a few supplementary statements should be added.

The families of the thyroidectomized series (fig. 20, part I) were all very similar. Thyroidectomized males showed no sex activity, so that it was necessary to mate normal stock males with thyroidectomized females. From these matings some offspring were produced, the litters ranging in size from four to seven of which three to four of each litter died before weaning time. This represents about one-third normal fertility. Male offspring of thyroidectomized females and normal males were mated with normal females. From these no offspring were produced. Still-births were common in the offspring of operated animals. The period of gestation was lengthened from 22 or 23 days to 30 or 32 days. Many of the animals were malformed; legs and tail shorter than normal and deformed ears and heads were among the malformations.

Animals which were injected with T. G. S. (without thyroidectomy) showed a slightly increased sex activity. Litters were of about normal size. No malformations were noted in the

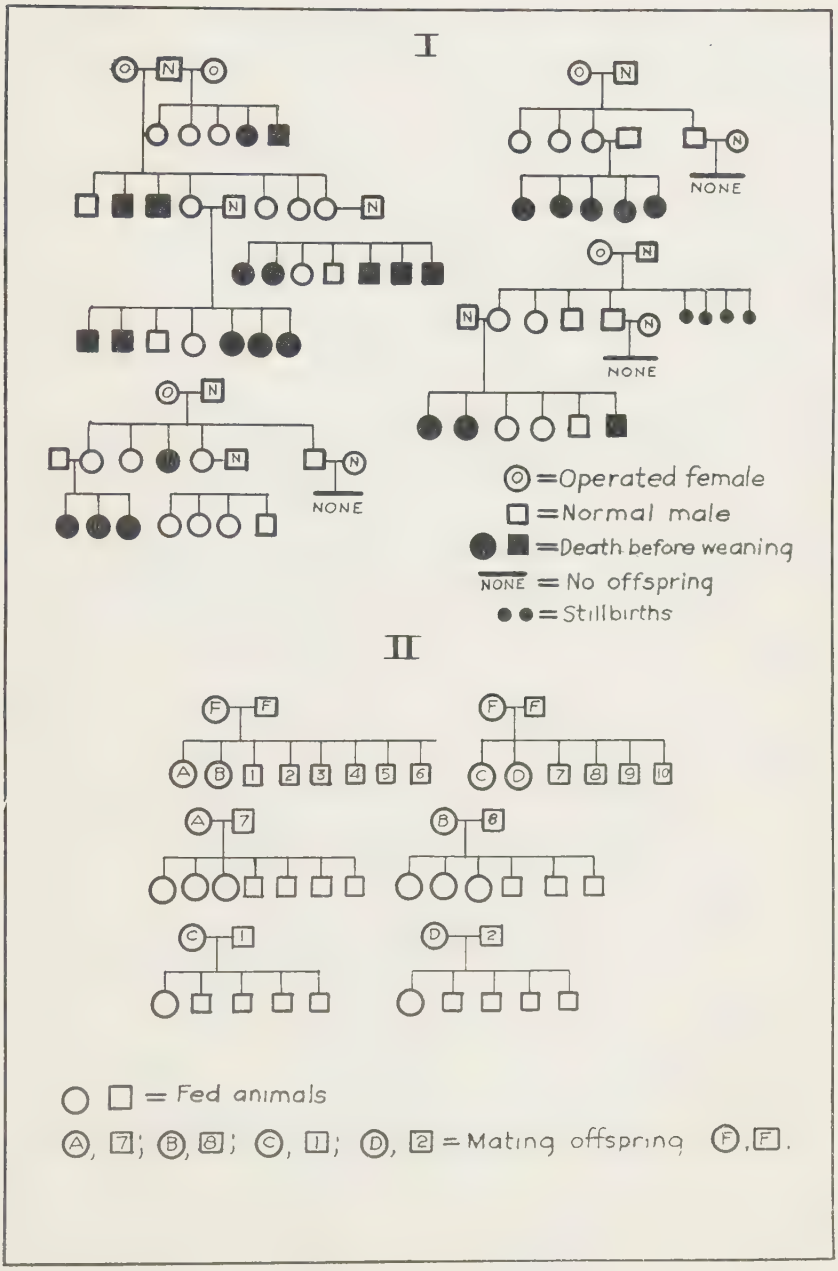
I
NONE
NONE
NONE
O =Operated female
□ =Normal male
■ =Death before weaning
NONE = No offspring
●● =Stillbirths
II
○ □ = Fed animals
Ⓐ, 7; Ⓑ, 8; Ⓒ, 1; Ⓓ, 2 = Mating offspring Ⓕ, F.

FIG. 20

offspring with the exception of a slight reduction in size and a tendency toward protruding eyes. Part II of figure 20 shows the typical family of this group.

XII. GENERAL CONCLUSIONS

1. The amount of thyroid gland substance which the normal animals used in this experiment are able to take (tolerate), with the maintenance of apparently normal health, increases with age. For animals below 50 days the amount, when fed, is from 0.30 to 0.50 gram daily; for animals over 50 days the amount is from 0.60 to 0.80 gram.

2. Thyroid gland substance fed in excess of toleration produces symptoms of languor, inactivity, hyperactivity, increased respiration, increased pulse, vaso-motor disturbances, difficulties of locomotion, and death.

3. When younger than 50 days, feeding thyroid gland substance produced an enlargement of the thyroid gland; such enlargement did not occur in animals over 50 days old when treatment was begun.

4. To produce the same behavior effects, the animals could tolerate about twice as much T. G. S. when fed by mouth as when injected.

5. Thyroidectomy causes a progressive incoördination of behavior, in that the movements become slower, less stable, and meaningless. There was also a loss of whatever preoperative learning or skill had been acquired. The vitality was reduced, sensitivity decreased, and a progressive deterioration of the vegetative processes was begun. These effects were more pronounced in younger animals. In the males sex activity disappeared, but the females did not become sterile.

6. Small amounts of T. G. S. *injected* into the animals caused no apparent change in general health, but the animals became hyperactive when in the maze and all learning or improvement in the skill and accuracy in behavior was practically impossible. The skill which had been acquired was lost. There gradually develops a swift and meaningless jumping about, and, instead of a dropping off of useless movements, the number of errors actually increase.

The instability and hyperactivity increase both in the maze and in the home cages. The age factor again presents itself in that the effects of T. G. S. injections are less pronounced with age.

7. In general the *feeding* of T. G. S. results in the same loss of skill and accuracy, which is proportional to the amount fed and inversely proportional to the age of the animals, as was indicated where T. G. S. was injected. The movements become more rapid but less coördinated; the effects of previous coördination gradually vanish in erratic and convulsive forms of behavior, and learning new responses seems impossible.

8. Normal males mated with thyroidectomized females produced offspring which were small, underweight, and had locomotor and vasomotor deficiencies. The performance level could hardly be compared with the performance of the offspring of normal animals. A maze performance of one minute by a normal offspring, required thirty minutes by the offspring of a thyroidectomized female. However, when the first generation offspring of thyroidectomized females were fed T. G. S., their learning and behavior condition rapidly approached that of normal offspring both in maze performance and in general vitality, although there was very little increase in size.

9. The offspring of males and females being *fed* 0.70 gram T. G. S. during the period of breeding and gestation showed a very erratic and nervous behavior both around the home cages and in the maze. While the offspring themselves received no T. G. S. treatment and in appearance seemed normal, their learning ability, in the sense that their maze records improved with repetitions, had practically disappeared.

10. The offspring of parents which had been *injected* with T. G. S. were slightly smaller than normal animals and had protruding eyeballs. Without T. G. S. treatment their movements were jerky, and, while their maze records are about the same as that of normal rats at the beginning, they showed no improvement during the short time they served in the experiment.

11. When females (F_2), produced from thyroidectomized females and normal males (F_1), were mated with normal males, the offspring of these F_2 females were similar to the first genera-

tion (F_1) offspring of normal males and thyroidectomized females. They were small and underweight, and they had locomotor and vasomotor deficiencies. When these animals were treated with T. G. S. by injection, their learning ability improved to such an extent that their maze time dropped from about 30 minutes to 2 minutes. Their size, however, remained very much below normal.

12. The second generation of offspring from parents and grandparents which had been injected with T. G. S. were extremely active, unstable, and nervous. While there is some evidence of learning in the maze record, the experimental period is too short to justify any conclusion.

XIII. BREEDING AND CARE OF THE COLONY

The breeding stock for this work was obtained from the experimental colony at the Wistar Institute. The entire breeding stock was kept free from any thyroid modification. The colony at the Wistar is one which has been subjected to the "gentling" process by Dr. F. S. Hammett. This treatment has been of great value since parts of this study necessitated handling the animals a great deal.

The breeding cages were specially designed to make the routine care of the animals as convenient as possible and to insure the stock against disease and parasites. Two sets of trays, a movable wire mesh and a movable heavy tin, were provided for each cage. A two-inch wire screen was placed at the top of the back to provide good ventilation. Nests of wood, wool and paper were used. The living quarters of the animals were kept at a very nearly constant temperature of 70 to 72 degrees.

The general diet consisted of the "table scraps" menu used at the Wistar Institute. A balanced ration was given to all animals both the breeding stock and these undergoing thyroid treatments.

It frequently happened that mothers with their first litters would eat up the young. This was combated by an addition of fresh meat and more green vegetables to their diet. The average sized litter for the normal animal was from eight to ten. Litters containing less than four animals were discarded.

The animals were bred at about five months of age. They were mature at this age and raised all of the litter brought forth.

REFERENCES

(1) Abelin, J.: Beiträge zur Physiologie der Drüsen. Leon Ascher. XXIX. Nachweis der Stoffenwechselwirkung der Schildrüse mit Hilfe eines Eiweissfreien, oder jodarmen Schildrüsen-praparatus. Zeitschr. f. Biochem. (Oldenberg), 1917, lxx, 259.

(2) Allen, B. M.: The effects of thyroid removal upon the development of the gonads in the larvae of Rana pipiens. Science, n.s., xlvi, 216, 1917.

(3) Backman, E. L.: Beiträge zur Physiologie der Drüsen. Leon Ascher. XXX. Untersuchungen zur Frage ob nach Extirpation von Schildrüse und Nebenschildrüsen biologisch nachweisbare toxische Stoffe im Blute auftretten. Zeitschr. f. Biolog. München, 1917, lxvii, 353.

(4) Bandler, S. W.: The Endocrines. W. B. Saunders Co., 1921.

(5) Bardeleben: C. R. de l'Academie des Sciences, 1884, 361.

(6) Bassett, G. C.: Habit formation in a strain of white rats with less than normal brain weight. Behavior monographs, No. 4, ii.

(7) Beidl, A.: Innere Sekretion, Auf. 2, Berlin, 1917.

(8) Cameron, A. T.: Biochemistry of iodine. IV. The effect of thyroxin on growth in white rats and rabbits. Jour. Biol. Chem., 1921, xlvi, 35.

(9) Cameron, A. T., and Carmichael, J.: Effect of parathyroid and thyroid feeding in the white rat. Amer. Jour. Physiol., 1921, lviii, 1.

(10) Cameron, A. T., and Carmichael, J.: Biochemistry of iodine. III. The comparative effects of thyroidectomy and iodide feeding on growth in white rats and rabbits. Jour. Biol. Chem., 1920, xlv, 69.

(11) Cameron, A. T., and Sedziak: Effect of thyroid feeding on adult white rats. Amer. Jour. Physiol., 1921, lviii, 7.

(12) Cannon and Cattell: Studies on the conditions of activity in the endocrine glands. II. The secretory innervation of the thyroid gland. Amer. Jour. Physiol., 1916, xli, 58.

(13) Colzi: Lo Speriment, 1884, xxxviii, 36.

(14) Cooper, A.: Guy's Hospital Report, 1836, 454.

(15) Cunningham, R. H.: Experimental thyroidism. Jour. Exper. Med., 1898, iii, 6.

(16) Cristiani, H.: Recherches sur le corps thyroide du rat. Rev. Med. de la Suisse Rom., 1892, xii, 729.

(17) Crotti, Andre: Thyroid and Thymus. Lea and Feibiger, Philadelphia.

(18) Cruveilheir: Anatomie Descriptive, 1834, ii, 691.

(19) Dashiell, J.: Need for analytical study of the maze problem. Jour. Psychobiol., 1920, ii, 181.

(20) Dashiell, J.: Some transfer factors in maze training by the white rat. Jour. Psychobiol., 1920, ii, 329.

(21) Dashiell, J.: Comparison of complete vs. alternate methods of learning two habits. Psychol. Rev., 1920, xxvii, 112.

(22) Degener, Lyda May: Studies on the effect of diet on the weight of the hypophysis and thyroid gland of the albino rat, and on the action of their extracts on the isolated small intestine. Amer. Jour. Physiol., 1922, lx, no. 1, 107.
(23) Donaldson, H. A.: The Rat. Memoirs of the Wistar Institute, No. 6, 1915.
(24) Drobnick: Arch. f. Exp. Path. u. Pharm., 1888, xxv, 136.
(25) Dubois, M.: Physiologie der Drüsen. Leon Ascher. XXXI. Ueber das Zuzammenwerken von Milz, Schildrüse und Knockenmark. Biochem. Ztschr., Berlin, 1917, lxxii, 141.
(26) Edmunds, W.: Effects of thyroid feeding on monkeys. Proc. Roy. Soc., no. 420, 368.
(27) Edmunds, W.: Further observations on the thyroid gland. VI. Jour. Pathol. Bact., xii, 101.
(28) Edmunds, W.: Eye effects following experimental thyroidectomy. Ophthalmoscope, xiv, 300.
(29) Ewald, J. R.: Berl. Klin. Wochenschr., 1887, 179.
(30) Ewald, J. R.: Berl. Klin. Wochenschr., 1889, 321.
(31) Farrant, R.: Hyperthyroidism, its experimental production in mammals. Brit. Med. Jour., ii, 50.
(32) Fuhr, F.: Arch. f. Exp. Path. u. Pharm., Leipzig, 1886, xxi, 387.
(33) Fuhr, F.: Arch. f. Exp. Path. u. Pharm., Leipzig, 1889, xxv, 363.
(34) Gley, E.: The theory of internal secretions: Its history and development. Practitioner, London, 1915, xciv, 2.
(35) Gley, E.: Gas. de Paris, 1891, no. 43.
(36) Gley, E.: Archiv. de Physiol., 1892, lxxxi, 295.
(37) Gley, E.: C. R. Soc. de Biol., 1893, no. 8, 217.
(38) Gley, E.: C. R. Soc. de Biol., 1895, no. 11, 216.
(39) Gley, E.: Arch. de Physiol., 1893, lxxxii, 467.
(40) Gley, E.: Pflügers Archiv., 1897, xvii, no. 76, 101.
(41) Gley, E.: C. R. Soc. de Biol., 1910, lxviii, 858.
(42) Gley, E.: C. R. Soc. de Biol., 1911, lxxx, 960.
(43) Gley, E.: Rev. Genei. des Sciences, January, 1898.
(44) Gudernatsch, J. F.: Feeding experiments on rats (thyroid). Anat. Rec., 1915, 78.
(45) Gudernatsch, J. F.: Feeding experiments on tadpoles (thyroid). Archiv. f. Ent., 1912, cxxxv, 40.
(46) Gudernatsch, J. F.: Feeding experiments on tadpoles (thyroid). II. Amer. Jour. Anat., 1914, xv, 12.
(47) Hammett, F. S.: Temperament and bodily constitution. Jour. Comp. Psychol., 1921, i.
(48) Hammett, F. S.: The thyroid apparatus. I. The stability of the nervous system as a factor in the resistance of the albino rat to the loss of the thyroid and parathyroid secretion. Amer. Jour. Physiol., 1921, lvi, 196.
(49) Hammett, F. S.: The thyroid apparatus. IX. Effects of the loss of the thyroid and parathyroid glands at 100 days of age on the growth in body length, body weight and tail length of the male and female albino rats. Amer. Jour. Physiol., 1923, lxiii, 216.

(50) Hammett, F. S.: The thyroid apparatus. XIII. The effects of thyroparathyroidectomy and parathyroidectomy at 100 days of age on the reproduction system of male and female albino rats. Amer. Jour. Anat., 1923, xxxii, 37.
(51) Hammett, F. S.: The thyroid apparatus. XIV. The effects of thyroparathyroidectomy and parathyroidectomy at 100 days of age on the growth of the glands of internal secretion. Amer. Jour. Anat., 1923, xxxii, 53.
(52) Halpenny, J., and Thompson, F. D.: On the relationship between the thyroids and parathyroids. Anat. Anz., 1909, xxxiv, S. 376.
(53) Halpenny, J., and Gunn, John A.: Note on extirpation of the thyroid gland in monkeys. Quart. Jour. Exper. Physiol., 1911, iv, 327.
(54) Handfield-Jones: Article in Todd's Cyclopedia of Anatomy and Physiol. 1849–1852, vol. 4, part 2, pp. 1117.
(54a) Heron, W. T.: Individual differences in ability versus chance in the learning of the stylus maze. Comp. Psychol. Mon., 1924, ii, no. 8.
(55) Herrman, C.: Three children with sporadic cretinism in one family. Arch. Pediat. (N. N.), 1917, xxix, 6.
(56) Herring, P. T.: Action of thyroid on growth of the body and organs of the white rat. Quart. Jour. Exper. Physiol., 1917, xi, 231.
(57) Hewitt, J. A.: The effects of administering small amounts of thyroid gland on the size and weight of certain organs in the male white rat. Quart. Jour. Exper. Physiol., 1918–20, xii, 347.
(58) Hewitt, J. A.: The influence on metabolism of administering small amounts of thyroid gland and the anterior lobe of the pituitary. Quart. Jour. Exper. Physiol., 1915, viii, 195, part 1.
(59) Hewitt, J. A.: Same as above. 1915, Part II.
(60) Howell, William H.: A textbook of Physiology. W. B. Saunders, Philadelphia, 1920, 873.
(61) Hoskins, E. R.: The growth of the body and the organs of the albino rat as affected by the feeding of various ductless glands, thyroid, thymus, hypophysis and pineal. Jour. Exper. Zoöl., xxi, 295.
(62) Hoskins, E. R., and Hoskins, M. M.: Growth and development of amphibia as affected by thyroidectomy. Jour. Exper. Zoöl., 1919, xxix, 1.
(63) Hoskins, R. G.: Congenital thyroidism (guinea pigs). Amer. Jour. Physiol., xxvi, 311.
(64) Huber, G. Carl: The development of the albino rat. Jour. Morphol., 1915, xxvi, 247.
(65) Hubbert, H. B.: The effect of age on habit formation in the albino rat. Behavior Mon., 1915, ii, No. 6.
(65a) Hunter, W. S., and Randolph, Vance: Further studies on the reliability of the maze with rats and humans. Jour. Comp. Psychol., 1924, iv, 431.
(66) Janney, N. W.: Anabolic action of the thyroid gland. Proc. Amer. Soc. Biol. and Chem. Jour. (N. Y.), 1917, xxix, 6.
(67) Janney, N. W., and Henderson, H. E.: Concerning the diagnosis and treatment of hypothyroidism. Arch. Int. Med., 1920, xxvi, 297.
(68) Kendall, E. C.: The function of the thyro-parathyroid apparatus. Jour. Amer. Med. Assoc., 1916, lxvi, 811.

(69) Kendall, W.: The relation of the thyroid to the other ductless glands. Lancet, 1917, xxxvii, 768.
(70) Klinkert, H.: Myxoedema. Ned. Tydschr. v. Geneesk. Haarrlem, 1921, lxv, 467.
(71) Kojima, Masaharii: Studies on endocrine glands. III. The effect on the thyroid and parathyroid of the rat of administering thyroid extract and certain other autocoids and salts. Quart. Jour. Exper. Physiol., 1917, xi, 339.
(72) Krogh, M.: Influence of thyreodin on standard metabolism. Ugesk. f. Laeger, Kobenhaun, 1916, lii, 4.
(73) Lashley, K. S.: Criterion of learning in experiments with the maze. Jour. Animal Behavior, 1917, vii, 66.
(74) Lenhart, C. H.: The influence upon tadpoles of feeding desiccated thyroid gland in variable amounts and of variable iodine contents. Jour. Exper. Med., 1915, xxii, 10.
(75) Levin, S.: One thousand one hundred and forty-six goiters in one thousand, seven hundred eighty-three persons. Arch. Int. Med., 1912, xxvii, 421.
(76) Liddell, Howard: The effect of thyroidectomy on the intelligence of sheep. Proc. Soc. Exper. Biol. and Med., 1922, xix, 343.
(77) Liddell, Howard: Some methods for investigating the effect of thyroidectomy on the neuro-muscular mechanism of sheep. Quart. Jour. Exper. Physiol., 1923, xiii, 191.
(78) Livingston, A. E.: Effect of thyroidectomy followed by thyroid feeding on the weight of the pituitary in rabbits. Proc. Soc. Exper. Biol. and Med., 1914, xi, 320.
(79) Loeb, L.: Studies on compensatory hypertrophy of the thyroid gland. V. The effect of the administration of thyroid, thymus gland and tethelin and of a meat diet on the hypertrophy of the thyroid gland in guinea pigs. Jour. Med. Research, Boston, 1920, xlii, 77.
(80) Long, J. A., and Evans, H. McL.: The oestrous cycle in the rat and its associated phenomena. Univ. Calif. Pub., 1922, vi, Univ. Calif. Press, Berkeley.
(81) McCarrison: The Thyroid Gland. Wm. Wood and Co., N. Y., 1917.
(82) Magnus-Levy: Ueber den Respirationischen Gaswechsel unter den Einfluss der Thyreodea, Berl. Klin. Wochenschr., 1895, Nr. 30, 650.
(83) Marine, David: Functions of the thyroid gland. Physiol. Rev., 1922, xi, 326.
(84) Meissner, R.: Myxoedem mit Pluriglandular Insuffziens. Munchen. med. Wchnschr., xlviii, S. 488–490.
(85) Morgagni: Advers. Anat., 1718, Lib. vii, Cap. xxvi, 34.
(86) Moussu, H.: Influence de l'Alimentation thyroidienne sur Croissance reguliere. C. R. Soc. Biol., Paris, T. 51 (Dogs).
(87) Munk: Sitz. d. k. Press. Akad. der Wiss., 1887, 823.
(88) Munk: Sitz. d. k. Press. Akad. der Wiss., 1888, 1059.
(89) Philipeux: C. R. Soc. de Biol., Paris, 1884, 8 Nr., 823.
(90) Raynard: C. R. des Travaux de l'Ecole Royale Veterinaire de Lyon. Pendant 18 Annee Scholaire, 1834, Recueil de Med. Vet. Pratique, 1835, xiii, 8.

(91) Rudunger, C., Falta, W., and Eppinger, H.: Ueber die wechselwirkung der Drüsen mit inneren Sekretion. Zeit. Klin. Med., lxvi, 102.
(92) Sajous, Charles E. de M.: The Internal Secretions and the Principles of Medicine. Vol. I. The Functions and Diseases of the Ductless Glands. F. A. Davis Co., Philadelphia, 1919.
(93) Santorini: Observ. Anat., Venetiis, October, 1724, vi, Art. XVII, 114.
(94) Schaefer, E. A.: The Endocrine Glands. Longmans, Green and Co., 1918.
(95) Schaefer, E. A.: Effects upon growth and metabolism of the addition of small amounts of ovarian tissue, pituitary and thyroid extract to the normal dietary of white rats. Quart. Jour. Exper. Physiol., 1912, v, 203.
(96) Schiff: Untersuch. ueber die zuckerbildung, Würzb., 1859, 361.
(97) Schiff: Revue Med. de la Suisse Romande, 15 Fev., 1884, 66.
(98) Schiff: Archiv. fur exp. Pharm. u. Path., 1884, xviii, 25.
(99) Schiff: Internat. Physiol. Kongress, Basel, 1884, 49.
(100) Simpson, Sutherland: Age as a factor in the effects which follow thyroidectomy and thyro-parathyroidectomy in the sheep. Quart. Jour. Exper. Physiol., 1913, vi, 119.
(101) Simpson, Sutherland: Thyro-parathyroidectomy in the rabbit. Proc. Soc. Exper. Biol. and Med., 0000, xi, 320.
(102) Simon, J.: Phil. Trans., 1844, 251.
(103) Stahel: Deutsche Med. Wochenschr., Leipzig, 1887, 227.
(104) Toyofuku, Tamaki: Ueber die Parathyreaprive Veranderung des Rattenzahnes, Frank. Zeitschr. f. Path., 1911, viii, 249.
(105) Ulrich, J. L.: Integration of movements in learning in the albino rat. Psychobiology, 1920, ii, 375.
(106) Ulrich, J. L.: Distribution of effort in learning in the white rat. Behavior Mon., 0000, vol. 2, no. 4.
(107) Vassali, e Generali: Rivista di Patol. Nerv. e. Ment., 1896, I, fasc. iii and vii.
(108) Vassali, e Generali: Arch. Ital de Biol., 1900, xxxiii, 154.
(109) Veil, W. H.: Ueber das Verhalten der Genitalen Funktionen beim Myxoedema des Weibes., Arch. fur. Gyn. (Berlin), 1917, cvii, 199.
(110) Vincent, Swale: Internal Secretions and the Ductless Glands. Edward Arnold, 1912.
(111) Vincent, S., and Jolly, W. A.: Jour. Physiol., 1904, xxxii, 32.
(112) Vincent, S., and Jolly, W. A.: Jour. Physiol., 1906, xxxiv, 295.
(113) Vincent, S. B.: The white rat and the maze problem. Jour. Animal Behavior, 1915, v, 16.
(114) Von Cyon, E.: Zentralbl. f. Physiol., 1897, xi, 691.
(115) Von Eiselberg, A.: Ueber Wachstum-Stoerungen bei Thieren nach freuhzietiger Schildrüsen-Extirpation. Archiv. f. Klinische Chirugie, 1894-95, xlix.
(116) Von Eiselberg, A.: Verhandl. der Deutschen Geselsch. f. Chirugie, xxvi, Congress, 1893.
(117) Wagner: Wiener Med. Blätter, 1884, Nrs. 25 and 30.
(118) Watson, Chalmers: A note on the minute structure of the thyroid gland in the white rat. Quart. Jour. Exper. Physiol., 1909, ii, 26.

(119) Watson, J. B.: The circular maze with the camera lucida. Jour. Animal Behavior, 1914, iv, 50.
(120) Waldeyer: Berl. Klin. Wochenschr., 1887, 233.
(121) Welch: N. Y. Med. Record, July–December, 1888, xxxiv, 368.
(122) Wharton: Adenographia, sive Glandularium totius Corporis Descriptio. London, 1656, cap. xviii, 118.
(123) Wiltbank, R. T.: Transfer of training in white rats on various series of mazes. Behavior Mon., iv, 1919, no. 17.
(124) Wylie, H. H.: An experimental study of transfer of habits in the white rat. Psychol. Bull., 1918, xv, 42.
(125) Yerkes, R. M., and Kellogg, C.: The graphic method of maze recording. Jour. Animal Behavior, 1914, iv, 56.

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